

09/895,871

Do you want to switch to the Registry File?

Choice (Y/n):

Switching to the Registry File...

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.84	0.84

FILE 'REGISTRY' ENTERED AT 10:32:19 ON 30 DEC 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 29 DEC 2004 HIGHEST RN 805206-90-0
DICTIONARY FILE UPDATES: 29 DEC 2004 HIGHEST RN 805206-90-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>

Uploading C:\Program Files\Stnexp\Queries\895871.str

L1 STRUCTURE UPLOADED

=>

Uploading C:\Program Files\Stnexp\Queries\895871a.str

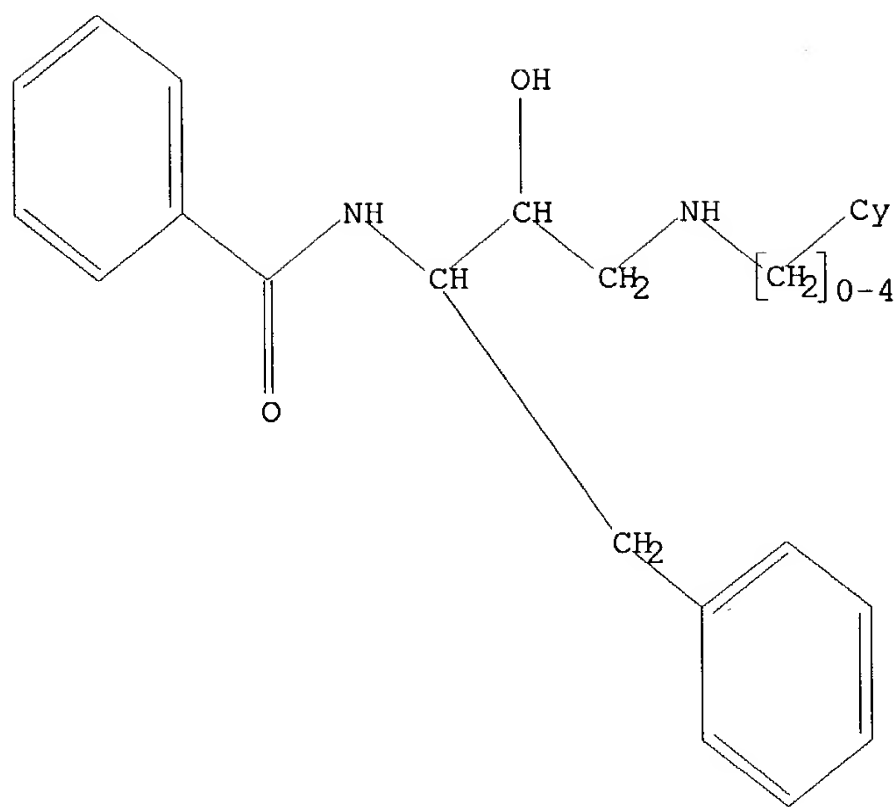
L2 STRUCTURE UPLOADED

=> d 11

L1 HAS NO ANSWERS

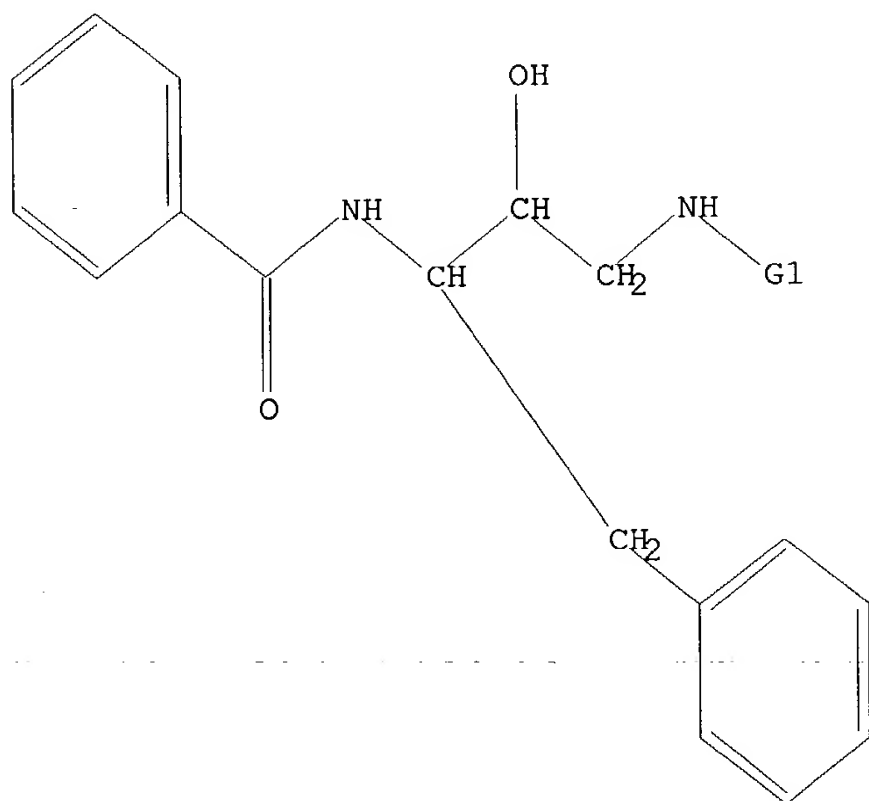
L1 STR

09/895,871



Structure attributes must be viewed using STN Express query preparation.

=> d 12
L2 HAS NO ANSWERS
L2 STR



G1 n-Pr, i-Pr, n-Bu, i-Bu, s-Bu, t-Bu

Structure attributes must be viewed using STN Express query preparation.

09/895,871

=> s l1 sss full
FULL SEARCH INITIATED 10:33:15 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 15317 TO ITERATE

100.0% PROCESSED 15317 ITERATIONS 2407 ANSWERS
SEARCH TIME: 00.00.01

L3 2407 SEA SSS FUL L1

=> s l2 sss full
FULL SEARCH INITIATED 10:33:23 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 15323 TO ITERATE

100.0% PROCESSED 15323 ITERATIONS 50 ANSWERS
SEARCH TIME: 00.00.01

L4 50 SEA SSS FUL L2

=> file caplus	SINCE FILE	TOTAL
COST IN U.S. DOLLARS	ENTRY	SESSION
FULL ESTIMATED COST	310.84	311.68

FILE 'CAPLUS' ENTERED AT 10:33:32 ON 30 DEC 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 30 Dec 2004 VOL 142 ISS 1
FILE LAST UPDATED: 29 Dec 2004 (20041229/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L5 22 L3

=> s l4
L6 7 L4

=> s l3 and l4
22 L3
7 L4
L7 7 L3 AND L4

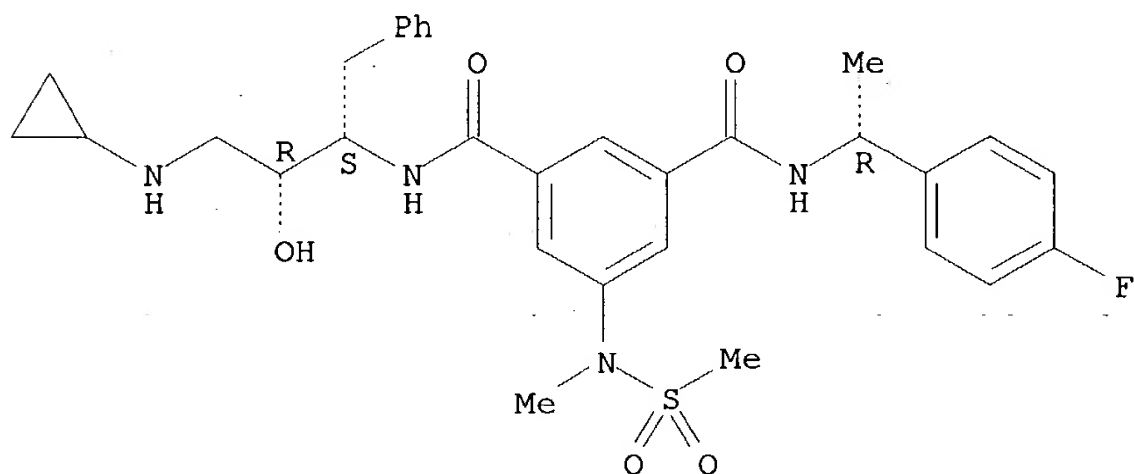
=> d l5 1-22 ibib abs hitstr

L5 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

09/895,871

ACCESSION NUMBER: 2004:956793 CAPLUS
TITLE: Structure-Based Design of Potent and Selective
Cell-Permeable Inhibitors of Human β -Secretase
(BACE-1)
AUTHOR(S): Stachel, Shawn J.; Coburn, Craig A.; Steele, Thomas
G.; Jones, Kristen G.; Loutzenhiser, Elizabeth F.;
Gregro, Alison R.; Rajapakse, Hemaka A.; Lai,
Ming-Tain; Crouthamel, Ming-Chih; Xu, Min; Tugusheva,
Katherine; Lineberger, Janet E.; Pietrak, Beth L.;
Espeseth, Amy S.; Shi, Xiao-Ping; Chen-Dodson,
Elizabeth; Holloway, M. Katharine; Munshi, Sanjeev;
Simon, Adam J.; Kuo, Lawrence; Vacca, Joseph P.
CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research
Laboratories, West Point, PA, 19486, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(26),
6447-6450
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We describe the development of cell-permeable β -secretase inhibitors
that demonstratively inhibit the production of the secreted amino terminal
fragment of an artificial amyloid precursor protein in cell culture. In
addition to potent inhibition in a cell-based assay ($IC_{50} < 100$ nM), these
inhibitors display impressive selectivity against other biol. relevant
aspartyl proteases.
IT 695216-22-9P 797035-11-1P 797035-13-3P
797035-17-7P 797035-18-8P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(structure-based design of potent and selective cell-permeable
inhibitors of human β -secretase (BACE-1))
RN 695216-22-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(1S,2R)-3-(cyclopropylamino)-2-hydroxy-1-
(phenylmethyl)propyl]-N'-[(1R)-1-(4-fluorophenyl)ethyl]-5-
[methyl(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)

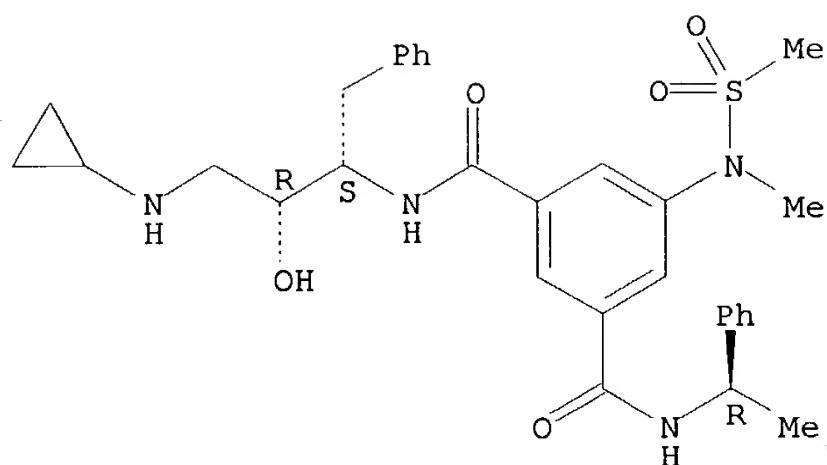
Absolute stereochemistry.



RN 797035-11-1 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

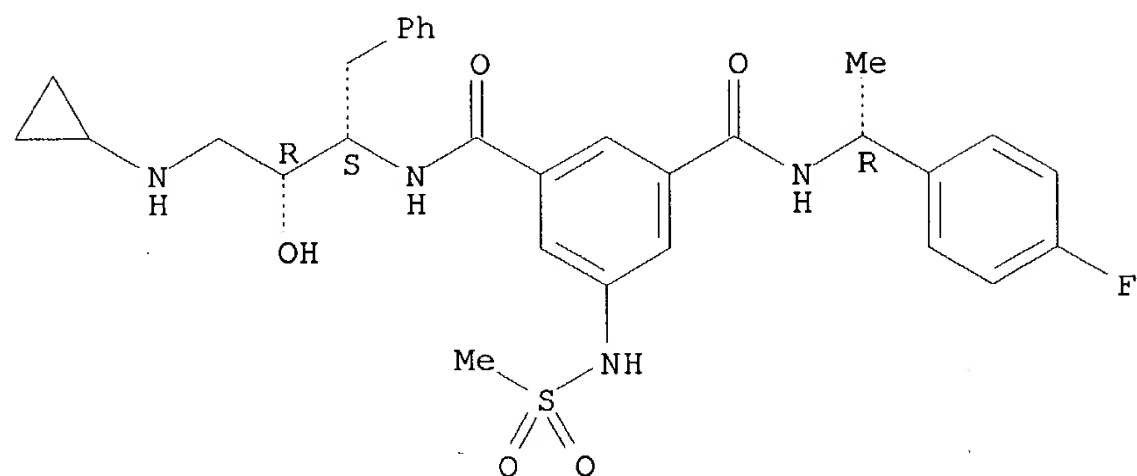
Absolute stereochemistry.

09/895,871



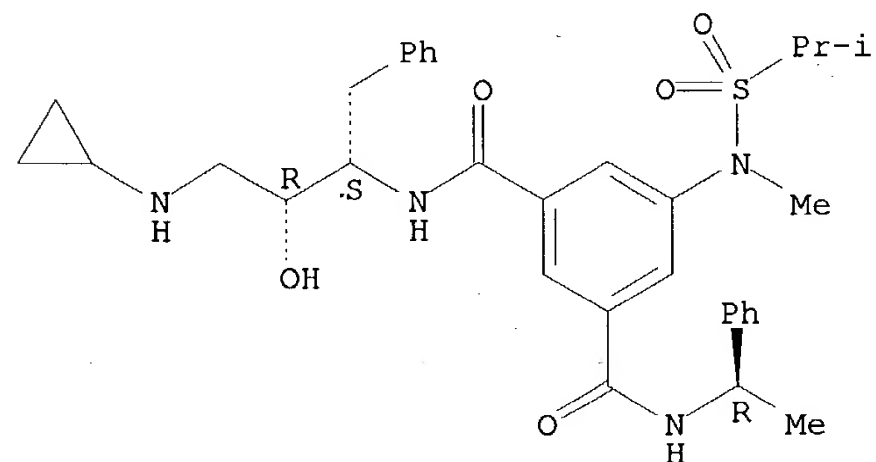
RN 797035-13-3 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



RN 797035-17-7 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

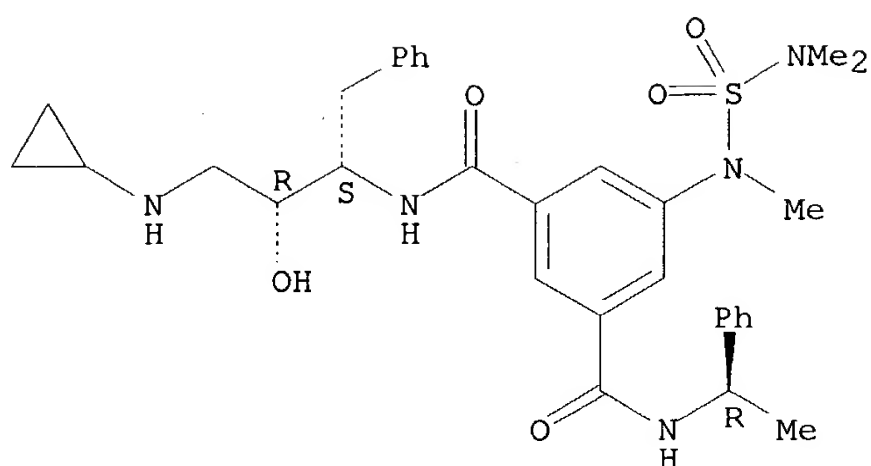
Absolute stereochemistry.



RN 797035-18-8 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

09/895,871



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:927212 CAPLUS

DOCUMENT NUMBER: 141:395588

TITLE: Preparation of hydroxydiaminopropyl tricyclic indolecarboxamides for treatment of β -amyloid related disease.

INVENTOR(S): Demont, Emmanuel Hubert; Redshaw, Sally; Walter, Daryl Simon

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 74 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094430	A1	20041104	WO 2004-EP4244	20040421
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

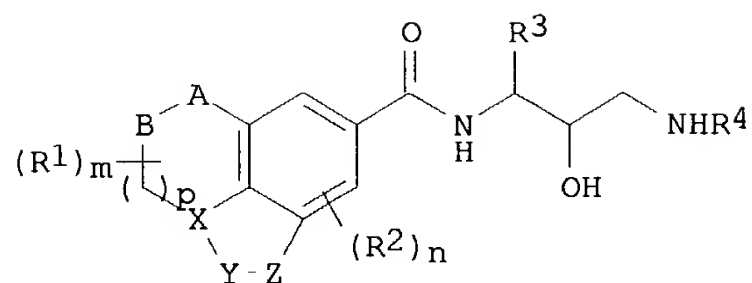
PRIORITY APPLN. INFO.:

GB 2003-9221

A 20030423

OTHER SOURCE(S): MARPAT 141:395588

GI



I

AB Title compds.[I; R1, R2 = alkyl, alkenyl, halo, alkoxy, amino, cyano, OH; m, n = 0-2; p = 1, 2; AB = NR5SO2, NR5CO; R5 = H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, aralkyl, heteroaralkyl, arylcycloalkyl, heteroaryl cycloalkyl; XYZ = NCR8:CR9; R8 = H, alkyl, cycloalkyl; R9 = R8, aryl, heteroaryl, aralkyl, heteroarylalkyl, etc.; R3 = (substituted) alkyl, alkenyl, alkynyl, alkylcycloalkyl, alkylaryl, alkylheteroaryl, alkylheterocyclyl; R4 = H, (substituted) alkyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, alkylcycloalkyl, cycloalkylaryl, heterocyclylaryl, etc.], were prepared Thus, 7-ethyl-2-oxo-1,2,3,4-tetrahydro[1,4]diazepino[3,2,1-hi]indole-9-carboxylic acid (preparation given), (2R,3S)-3-amino-1-(3-methoxybenzylamino)-4-phenylbutan-2-ol ditosylate, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, 1-hydroxybenzotriazole hydrate, and 4-ethylmorpholine were stirred 4 h in CH2Cl2/DMF to give 7-ethyl-2-oxo-1,2,3,4-tetrahydro[1,4]diazepino[3,2,1-hi]indole-9-carboxylic acid [(1S,2R)-1-benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]amide. I inhibited Asp-2 with IC50 <10 μ M.

IT 790252-01-6P 790252-02-7P 790252-03-8P
 790252-04-9P 790252-06-1P 790252-08-3P
 790252-10-7P 790252-12-9P 790252-20-9P
 790252-26-5P 790252-28-7P 790252-32-3P
 790252-34-5P 790252-36-7P 790252-38-9P
 790252-42-5P 790252-44-7P 790252-46-9P
 790252-48-1P 790252-50-5P 790252-56-1P
 790252-58-3P 790252-60-7P 790252-62-9P
 790252-64-1P 790252-66-3P 790252-68-5P
 790252-70-9P 790252-72-1P 790252-74-3P
 790252-75-4P 790252-78-7P 790252-81-2P
 790252-83-4P 790252-85-6P 790252-87-8P
 790252-89-0P 790252-91-4P 790252-93-6P
 790252-96-9P 790252-99-2P 790253-15-5P
 790253-26-8P 790253-29-1P 790253-32-6P
 790253-35-9P 790253-37-1P 790253-39-3P
 790253-41-7P 790253-43-9P 790253-45-1P
 790253-47-3P 790253-49-5P 790253-51-9P
 790253-55-3P 790253-57-5P 790253-59-7P
 790253-63-3P 790253-67-7P 790253-70-2P
 790253-79-1P 790253-82-6P 790253-84-8P
 790253-95-1P 790253-97-3P 790253-99-5P
 790254-01-2P 790254-03-4P 790254-05-6P
 790254-07-8P 790254-09-0P 790254-11-4P
 790254-12-5P 790254-15-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

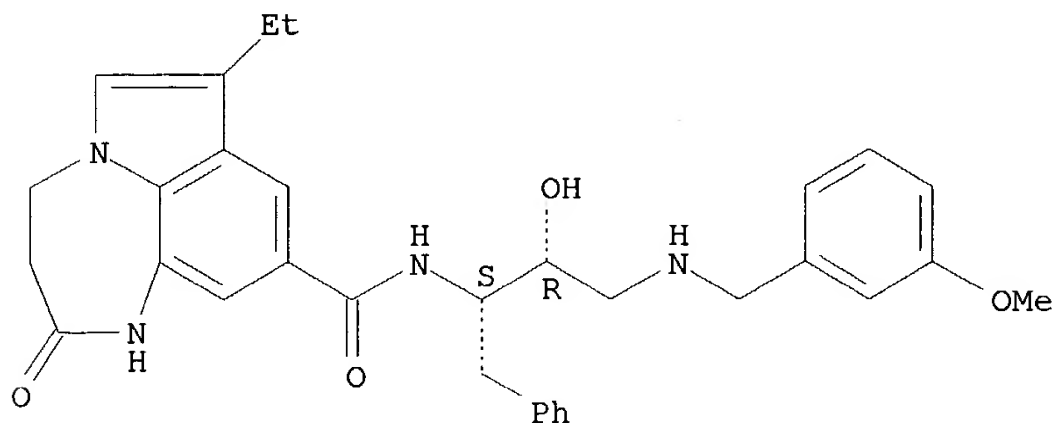
(preparation of hydroxydiaminopropyl tricyclic indolecarboxamides for treatment of β -amyloid related disease)

RN 790252-01-6 CAPLUS

09/895,871

CN Pyrrolo[1,2,3-ef]-1,5-benzodiazepine-9-carboxamide, 7-ethyl-1,2,3,4-tetrahydro-N-[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-2-oxo- (9CI) (CA INDEX NAME)

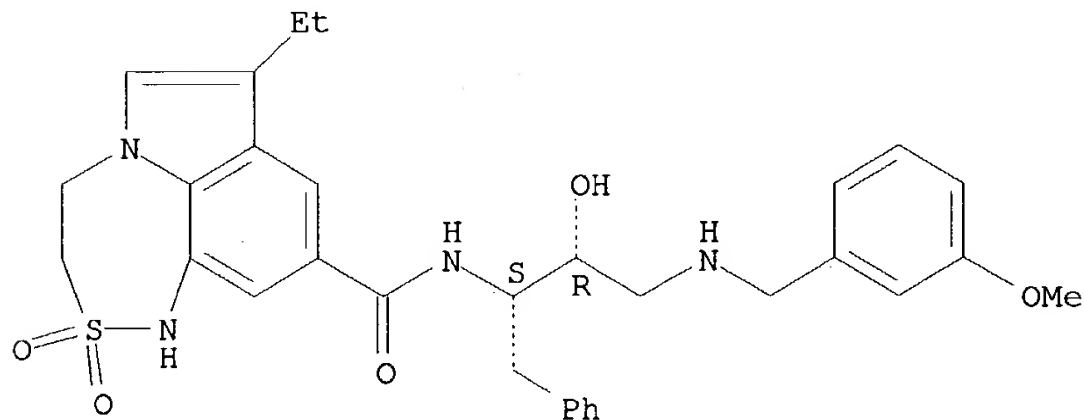
Absolute stereochemistry.



RN 790252-02-7 CAPLUS

CN 1H-Pyrrolo[1,2,3-ef]-2,1,5-benzothiadiazepine-9-carboxamide, 7-ethyl-3,4-dihydro-N-[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-, 2,2-dioxide (9CI) (CA INDEX NAME)

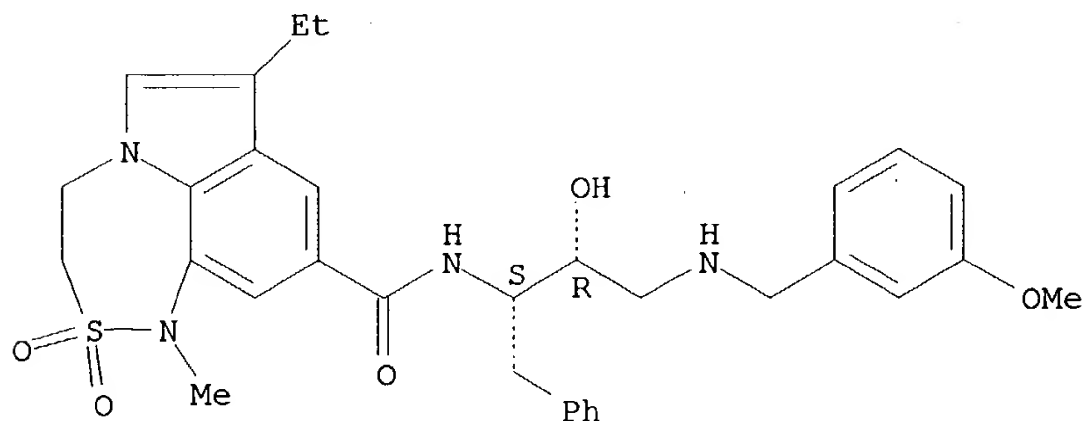
Absolute stereochemistry.



RN 790252-03-8 CAPLUS

CN 1H-Pyrrolo[1,2,3-ef]-2,1,5-benzothiadiazepine-9-carboxamide, 7-ethyl-3,4-dihydro-N-[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-1-methyl-, 2,2-dioxide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

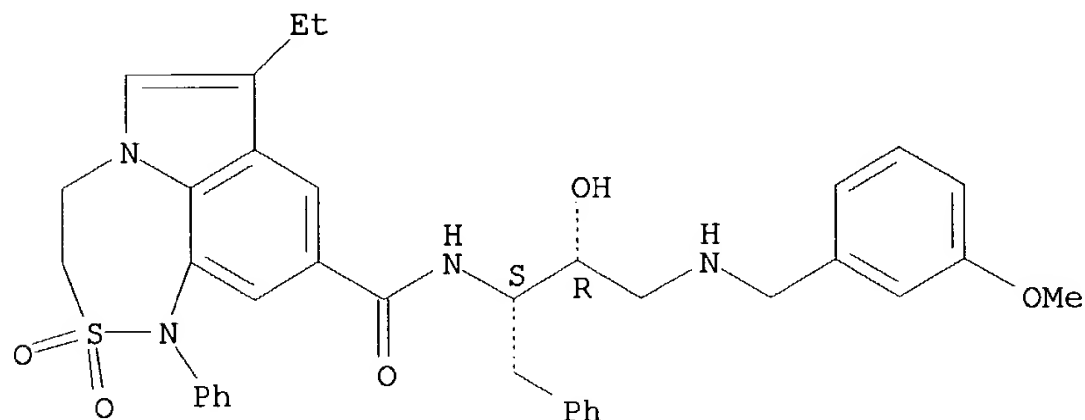


09/895,871

RN 790252-04-9 CAPLUS

CN 1H-Pyrrolo[1,2,3-ef]-2,1,5-benzothiadiazepine-9-carboxamide,
7-ethyl-3,4-dihydro-N-[(1S,2R)-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-1-phenyl-, 2,2-dioxide
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 790252-06-1 CAPLUS

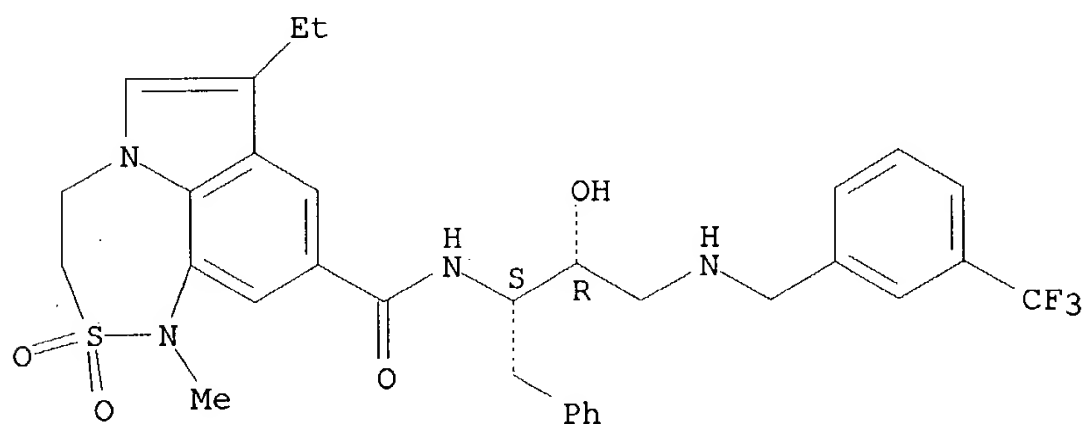
CN Formic acid, compd. with 7-ethyl-3,4-dihydro-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)phenyl)methyl]amino]propyl]-1-methyl-1H-pyrrolo[1,2,3-ef]-2,1,5-benzothiadiazepine-9-carboxamide
2,2-dioxide (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 790252-05-0

CMF C32 H35 F3 N4 O4 S

Absolute stereochemistry.



CM 2

CRN 64-18-6

CMF C H2 O2

O=CH-OH

RN 790252-08-3 CAPLUS

CN Formic acid, compd. with 7-ethyl-3,4-dihydro-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)phenyl)methyl]amino]propyl]-1,3-

09/895,871

CRN 64-18-6
CMF C H2 O2

O=CH-OH

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:927177 CAPLUS

DOCUMENT NUMBER: 141:395294

TITLE: Preparation of 2-hydroxy-3-aminoalkylbenzamides as
β-secretase inhibitors for the treatment of
Alzheimer's disease

INVENTOR(S): Aquino, Jose; John, Varghese; Tucker, John A.; Hom,
Roy; Pulley, Shon; Tenbrink, Ruth

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn
Company

SOURCE: PCT Int. Appl., 101 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

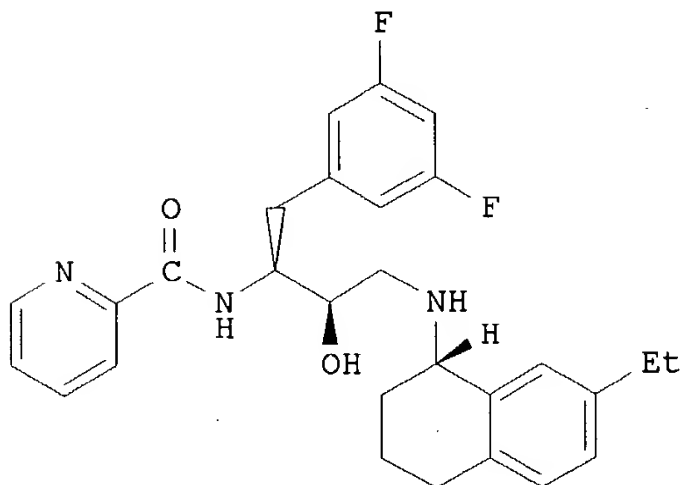
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094384	A2	20041104	WO 2004-US12197	20040421
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.:

US 2003-464687P P 20030421

GI



II

AB The present invention relates to 2-hydroxy-3-aminoalkylbenzamides, Z-X-NH-C(R1)-C(OH)-C(R2R3)-NR15Rc [I; Z = (un)substituted hetero/aryl, heterocyclyl; X = CO, SO2; R1 = (un)substituted alkyl; R2, R3 = independently H, F, (un)substituted alk(en/yn)yl, cycloalkyl; or R2CR3 = C3-C7-carbocycle, wherein one carbon is optionally replaced by O, S, SO2, etc.; R15 = H, (un)substituted alkoxy/hydroxy/halo/alkyl, alkoxy; Rc = (un)substituted (CH2)0-3-cycloalkyl, monocyclic or bicyclic ring, alkenyl, etc.] useful in treating Alzheimer's disease and similar diseases. These compds. include inhibitors of the beta-secretase enzyme (no data) that are useful in the treatment of Alzheimer's disease and other diseases characterized by deposition of A beta peptide in a mammal. The compds. of the invention are useful in pharmaceutical compns. and methods of treatment to reduce A beta peptide formation. 8 Synthetic examples of intermediates, characterization data for 11 examples, e.g. II, and another 18 claimed examples of I are included. General procedures for the preparation of compds. I are given. I displayed IC50 values < 50 μ M in a β -secretase inhibition assay. Selected I exhibited IC50 < 5 μ M in a cell free β -secretase inhibition assay.

IT **527731-85-7P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(4R)-6-ethyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl)amino]-2-hydroxypropyl]-3,5-dimethylbenzamide **527733-19-3P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(4R)-6-ethyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl)amino]-2-hydroxypropyl]-4-(2-methoxyethyl)benzamide **789490-77-3P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(4S)-6-neopentyl-3,4-dihydro-2H-chromen-4-yl)amino]propyl]benzamide **789490-78-4P**, N-[(1S,2R)-3-[(4S)-6-tert-Butoxy-3,4-dihydro-2H-chromen-4-yl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide **789490-79-5P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(4S)-6-neopentyl-1,2,3,4-tetrahydroquinolin-4-yl)amino]propyl]benzamide **789490-80-8P**, N-[(1S,2R)-3-[(4S)-6-tert-Butoxy-1,2,3,4-tetrahydroquinolin-4-yl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide **789490-81-9P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(1S)-7-neopentyl-1,2,3,4-tetrahydronaphthalen-1-yl)amino]propyl]benzamide **789490-82-0P**, N-[(1S,2R)-3-[(1S)-7-tert-Butoxy-1,2,3,4-tetrahydronaphthalen-1-yl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide **789490-83-1P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(4R)-6-neopentyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl)amino]propyl]benzamide **789490-84-2P**, N-[(1S,2R)-3-[(4R)-6-tert-Butoxy-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide **789490-85-3P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[[1-(3-neopentylphenyl)cyclohexyl]amino]propyl]benzamide **789490-86-4P**, N-[(1S,2R)-3-[[1-(3-tert-Butoxyphenyl)cyclohexyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide **789490-87-5P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[[1-(3-neopentylphenyl)cyclopropyl]amino]propyl]benzamide **789490-88-6P**, N-[(1S,2R)-3-[[1-(3-tert-Butoxyphenyl)cyclopropyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide **789490-89-7P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[[4-neopentyl-1,1'-biphenyl-2-yl)methyl]amino]propyl]benzamide **789490-90-0P**, N-[(1S,2R)-3-[[4-tert-Butoxy-1,1'-biphenyl-2-yl)methyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide **789490-91-1P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(2-neopentyl-9H-fluoren-9-yl)amino]propyl]benzamide **789490-92-2P**, N-[(1S,2R)-3-[(2-tert-Butoxy-9H-fluoren-9-yl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

09/895,871

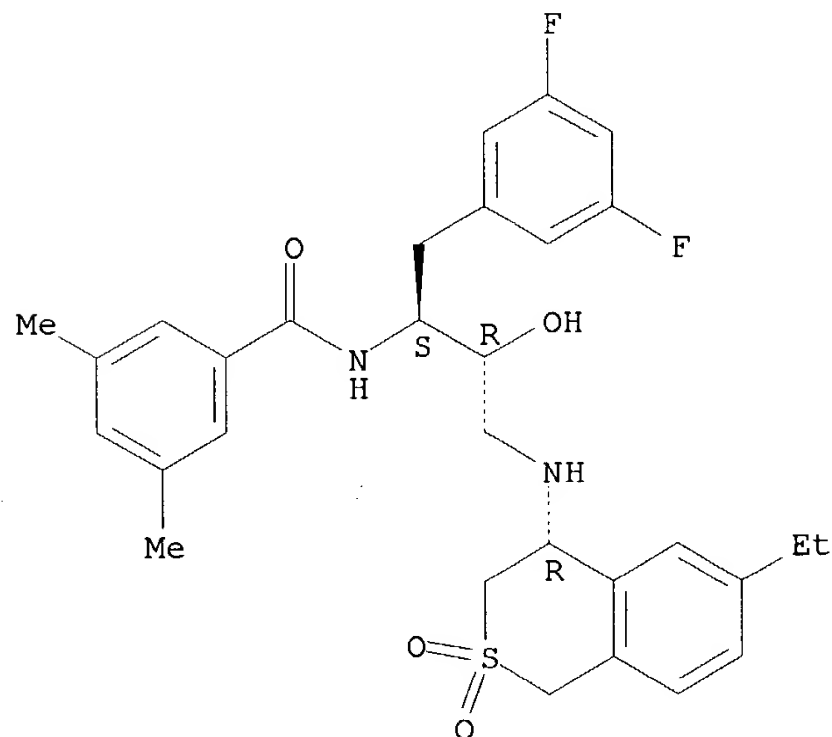
(Uses)

(drug candidate; preparation of 2-hydroxy-3-aminoalkylbenzamides as β -secretase inhibitors for treatment of Alzheimer's disease)

RN 527731-85-7 CAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(4R)-6-ethyl-3,4-dihydro-2,2-dioxido-1H-2-benzothiopyran-4-yl]amino]-2-hydroxypropyl]-3,5-dimethyl- (9CI) (CA INDEX NAME)

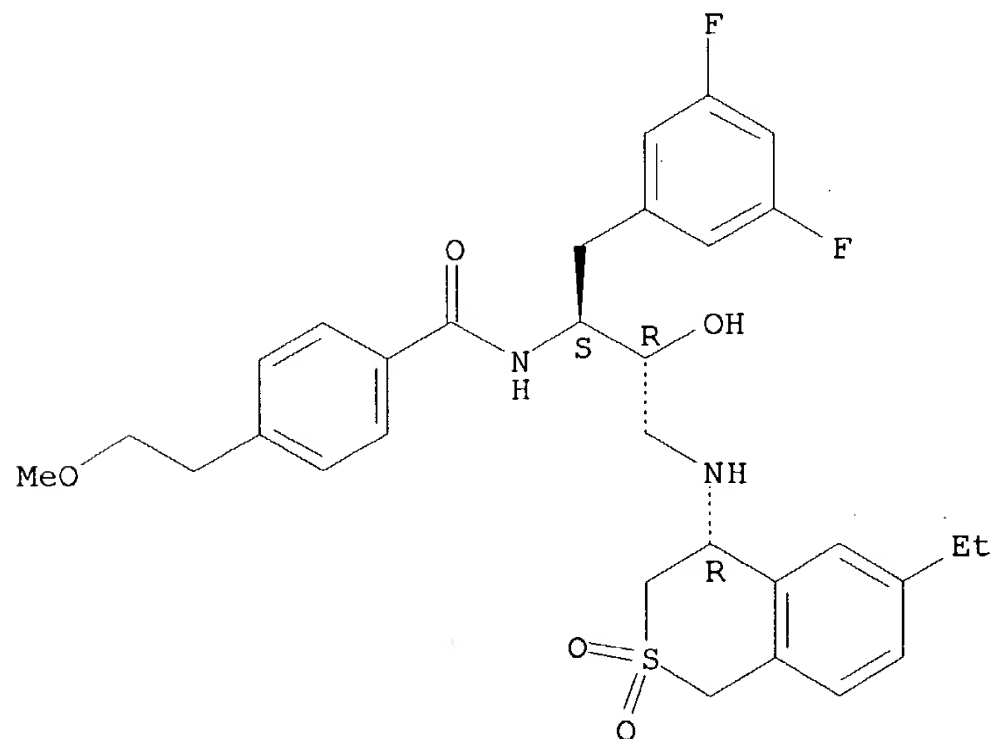
Absolute stereochemistry.



RN 527733-19-3 CAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(4R)-6-ethyl-3,4-dihydro-2,2-dioxido-1H-2-benzothiopyran-4-yl]amino]-2-hydroxypropyl]-4-(2-methoxyethyl)- (9CI) (CA INDEX NAME)

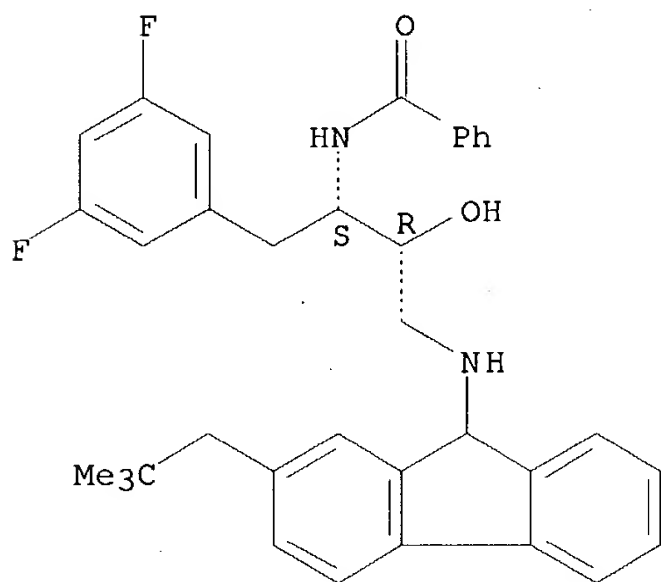
Absolute stereochemistry.



09/895,871

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[2-(2,2-dimethylpropyl)-9H-fluoren-9-yl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

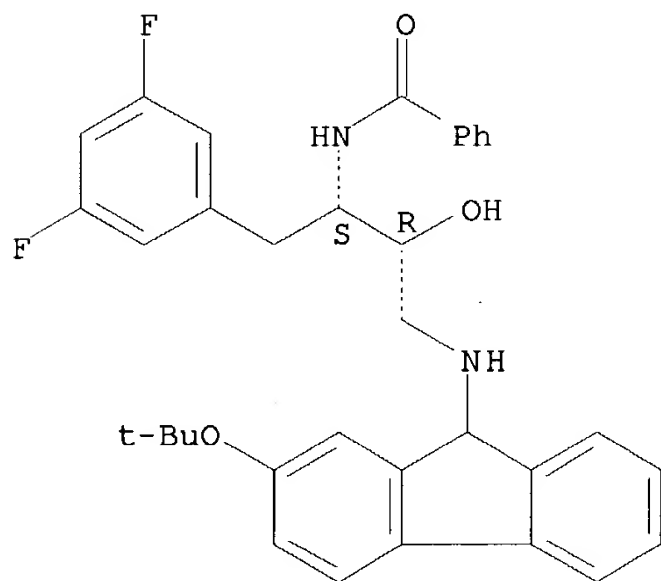
Absolute stereochemistry.



RN 789490-92-2 CAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[2-(1,1-dimethylethoxy)-9H-fluoren-9-yl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:788952 CAPLUS

DOCUMENT NUMBER: 141:421677

TITLE: Apo and Inhibitor Complex Structures of BACE (β-secretase)

AUTHOR(S): Patel, Sahil; Vuillard, Laurent; Cleasby, Anne; Murray, Christopher W.; Yon, Jeff

CORPORATE SOURCE: Astex Technology, Cambridge, CB4 0QA, UK

SOURCE: Journal of Molecular Biology (2004), 343(2), 407-416

CODEN: JMOBAK; ISSN: 0022-2836

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

09/895,871

LANGUAGE: English

AB Human BACE, also known as β -secretase, shows promise as a potential therapeutic target for Alzheimer's disease. The authors determined the apo structure of BACE to 1.75 Å, and a structure of a hydroxyethylamine inhibitor complex derived by soaking. These show significant active-site movements compared to previously described BACE structures. Addnl., the structures reveal two pockets that could be targeted by structure-based drug design.

IT **388062-23-5D**, complexes with aspartic proteinase BACE

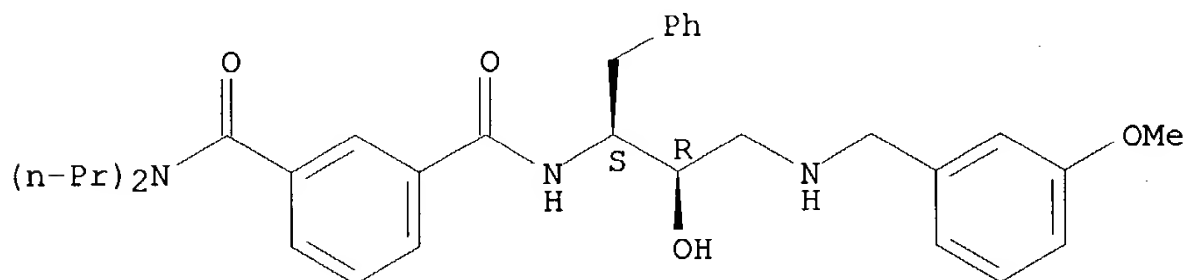
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(crystal structure of human β -secretase and complex with hydroxyethylamine inhibitor)

RN 388062-23-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'--[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:775885 CAPLUS

DOCUMENT NUMBER: 141:295745

TITLE: Preparation of hydroxyethylamine derivatives for the treatment of Alzheimer's disease

INVENTOR(S): Demont, Emmanuel Hubert; Redshaw, Sally; Walter, Daryl Simon

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080376	A2	20040923	WO 2004-EP2644	20040311
WO 2004080376	A3	20041111		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,			

09/895,871

ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG

PRIORITY APPLN. INFO.:

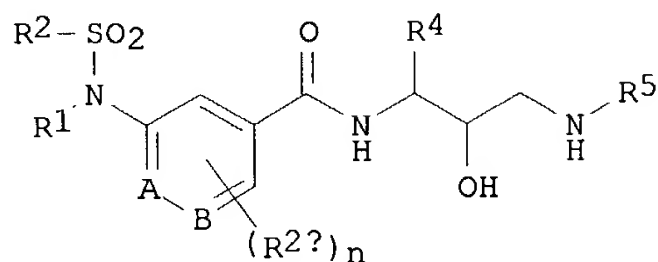
GB 2003-5918

A 20030314

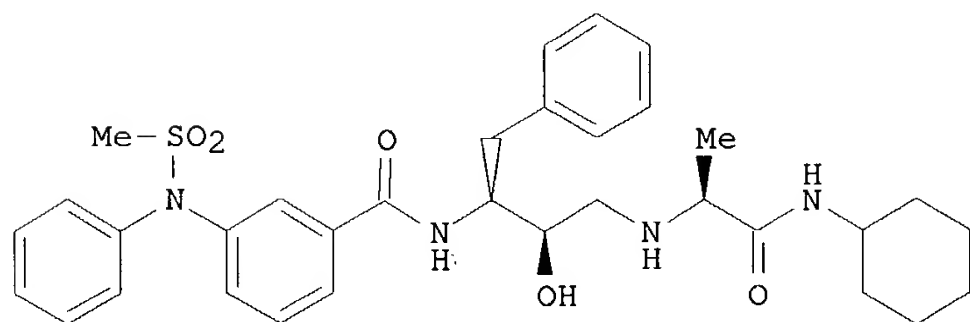
OTHER SOURCE(S):

MARPAT 141:295745

GI



I



II

AB The invention relates to novel hydroxyethylamine compds. I [R1 is aryl or heteroaryl; R2 is alkyl or cycloalkyl; R2a is H, halo, alkyl or alkoxy; n is 0-2; A is -CR2b= or -N=, where R2b is H, alkyl, alkenyl, halo, alkoxy, amino, cyano or hydroxy; B is -CR3= or -N=, where R3 is H, halo, (un)substituted alkyl, aryl, carboxy, etc.; R4 is alkyl, cycloalkyl-, aryl-, heteroaryl- or heterocyclalkyl; R5 is H, (un)substituted alkyl, aryl, -CRaRb-CONH-alkyl (Ra, Rb are H, alkyl or cycloalkyl), etc.] having Asp2 (β -secretase, BACE1 or Memapsin) inhibitory activity for use in the treatment of diseases characterized by elevated β -amyloid levels or β -amyloid deposits, particularly Alzheimer's disease. Thus, compound II was prepared by EDC/1-hydroxybenzotriazole-mediated coupling of 3-[(methanesulfonyl)phenylamino]benzoic acid with (S)-2-[(2R,3S)-3-amino-2-hydroxy-4-phenylbutylamino]-N-cyclohexylpropionamide dihydrogen chloride.

IT 761431-33-8P 761431-80-5P 761431-81-6P

761431-83-8P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

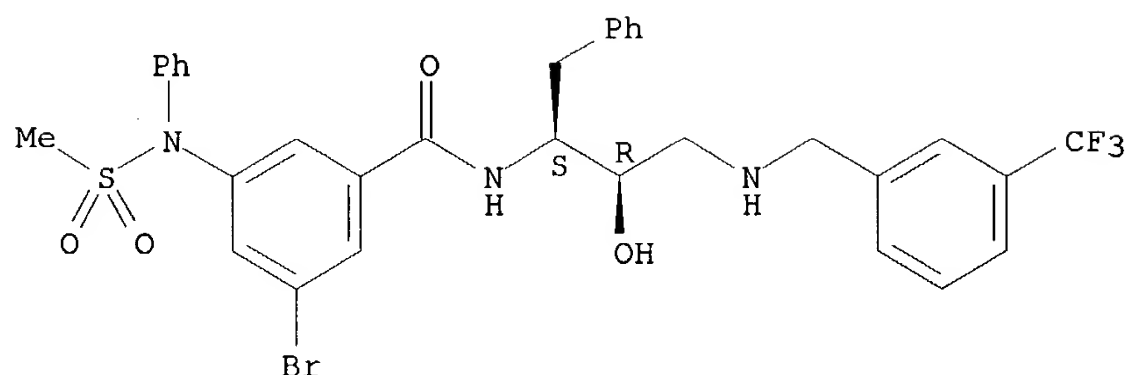
(preparation of benzoic acid hydroxyethylamide derivs. for treatment of Alzheimer's disease)

RN 761431-33-8 CAPLUS

CN Benzamide, 3-bromo-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)phenyl]methyl]amino]propyl]-5-[(methanesulfonyl)phenylamino]- (9CI) (CA INDEX NAME)

09/895,871

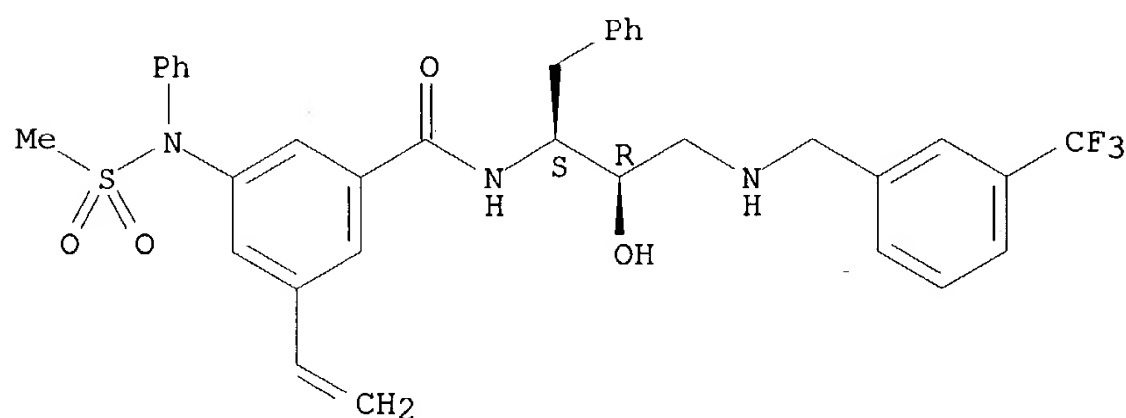
Absolute stereochemistry.



RN 761431-80-5 CAPLUS

CN Benzamide, 3-ethenyl-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)phenyl]methyl]amino]propyl]-5-[(methylsulfonyl)phenylamino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

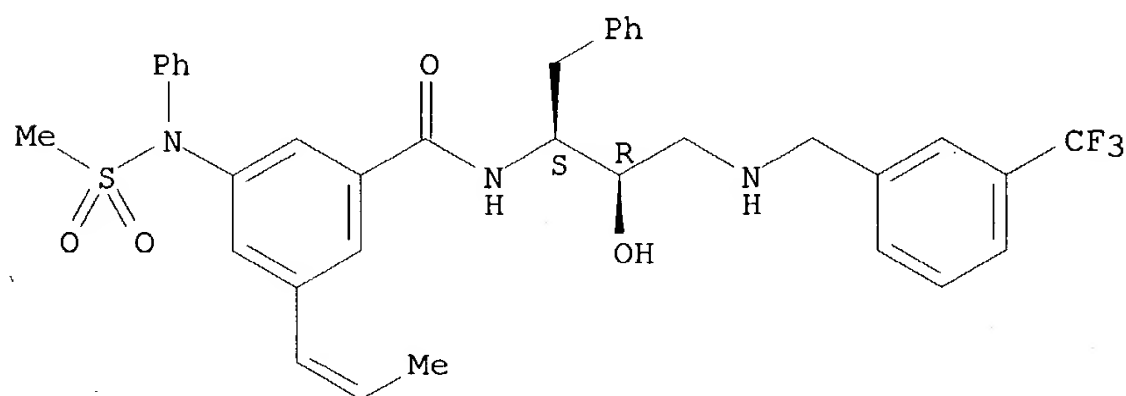


RN 761431-81-6 CAPLUS

CN Benzamide, N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)phenyl]methyl]amino]propyl]-3-[(methylsulfonyl)phenylamino]-5-(1-propenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

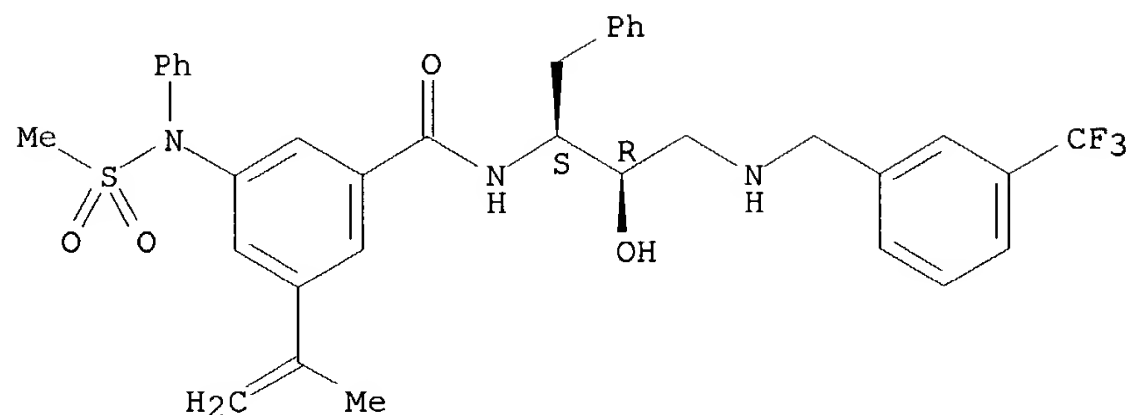


RN 761431-83-8 CAPLUS

CN Benzamide, N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)phenyl]methyl]amino]propyl]-3-(1-methylethenyl)-5-[(methylsulfonyl)phenylamino]- (9CI) (CA INDEX NAME)

09/895,871

Absolute stereochemistry.



IT 761431-01-0P 761431-02-1P 761431-03-2P
761431-04-3P 761431-05-4P 761431-06-5P
761431-07-6P 761431-08-7P 761431-10-1P
761431-11-2P 761431-12-3P 761431-13-4P
761431-16-7P 761431-17-8P 761431-18-9P
761431-19-0P 761431-23-6P 761431-24-7P
761431-25-8P 761431-28-1P 761431-30-5P
761431-32-7P 761431-34-9P 761431-35-0P
761431-36-1P 761431-37-2P 761431-38-3P
761431-39-4P 761431-42-9P 761431-44-1P
761431-46-3P 761431-48-5P 761431-49-6P
761431-50-9P 761431-51-0P 761431-52-1P
761431-55-4P 761431-56-5P 761431-57-6P
761431-58-7P 761431-59-8P 761431-60-1P
761431-62-3P 761431-64-5P 761431-66-7P
761431-68-9P 761431-70-3P 761431-72-5P
761431-74-7P 761431-76-9P 761431-78-1P
761431-79-2P 761431-82-7P 761431-84-9P
761431-85-0P 761431-86-1P 761431-87-2P
761431-90-7P

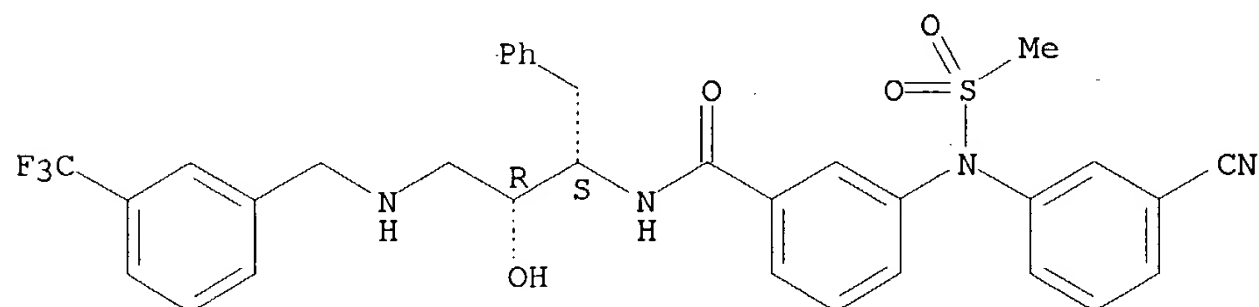
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of benzoic acid hydroxyethylamide derivs. for treatment of
Alzheimer's disease)

RN 761431-01-0 CAPLUS

CN Benzamide, 3-[(3-cyanophenyl)(methylsulfonyl)amino]-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)phenyl]methyl]amino]propyl]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 761431-02-1 CAPLUS

CN Benzamide, 3-[(3-chlorophenyl)(methylsulfonyl)amino]-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)phenyl]methyl]amino]propyl]-

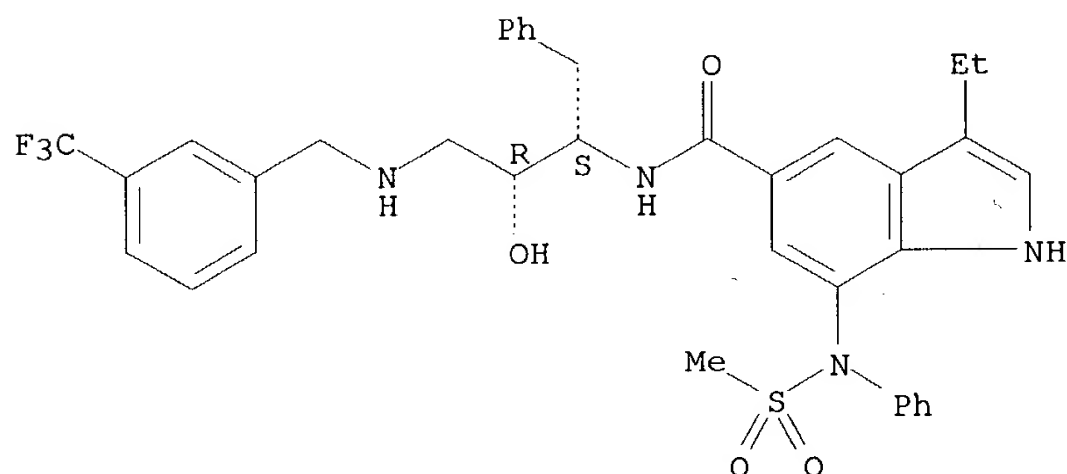
09/895,871

RN 761431-90-7 CAPLUS
CN Formic acid, compd. with 3-ethyl-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-
[[[3-(trifluoromethyl)phenyl]methyl]amino]propyl]-7-
[(methylsulfonyl)phenylamino]-1H-indole-5-carboxamide (1:1) (9CI) (CA
INDEX NAME)

CM 1

CRN 761431-89-4
CMF C36 H37 F3 N4 O4 S

Absolute stereochemistry.



CM 2

CRN 64-18-6
CMF C H2 O2

O=CH-OH

L5 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:493673 CAPLUS

DOCUMENT NUMBER: 141:54189

TITLE: Preparation of hydroxyethylamine derivatives for the
treatment of Alzheimer's disease

INVENTOR(S): Demont, Emmanuel H.; Faller, Andrew; MacPherson, David
Timothy; Milner, Peter Henry; Naylor, Alan; Redshaw,
Sally; Stanway, Steven James; Vesey, David R.; Walter,
Daryl S.

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 201 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004050619	A1	20040617	WO 2003-EP13806	20031203
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

09/895,871

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

GB 2002-28410

A 20021205

OTHER SOURCE(S): MARPAT 141:54189

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = alkyl, alkenyl, halo, etc.; R2' = H, alkyl, alkoxy, halo; m, n = 0-2; X = CO, SO, SO₂; p = 1-3; R2 = H, alk(en)yl, (hetero)aryl, etc.; R3 = halo, alk(en)yl, (hetero)aryl, etc.; R4 = alkynyl, alkylaryl, etc.; R5 = H, alkyl, cycloalkyl, cycloalkenyl, etc.] are prepared For instance, 5-(2-oxopyrrolidin-1-yl)-N,N-dipropylisophthalamide (preparation given) is coupled to (2S)-2-(((2R,3S)-3-amino-2-hydroxy-4-phenylbutyl)amino)-N-cyclohexylpropionamide (preparation given) (DMF, EDCI, HOBT, 4-ethylmorpholine, 3 h) to give II. Compds. of the invention inhibit protease Asp2 and Cathepsin D. I are useful in the treatment of diseases characterized by elevated amyloid levels or amyloid deposits, particularly Alzheimer's disease.

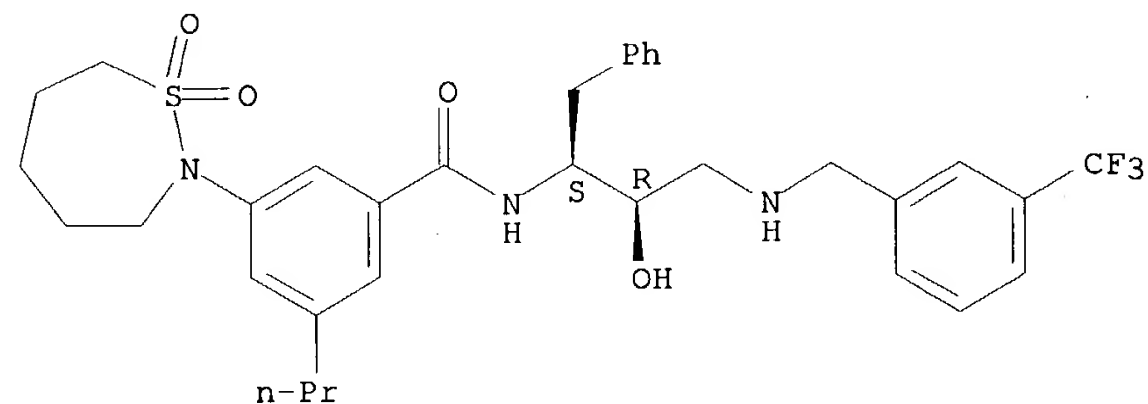
IT 706793-30-8P 706793-31-9P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of hydroxyethylamine derivs. for treatment of Alzheimer's disease)

RN 706793-30-8 CAPLUS

CN Benzamide, N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)phenyl]methyl]amino]propyl]-3-propyl-5-(tetrahydro-1,1-dioxido-1,2-thiazepin-2(3H)-yl)- (9CI) (CA INDEX NAME)

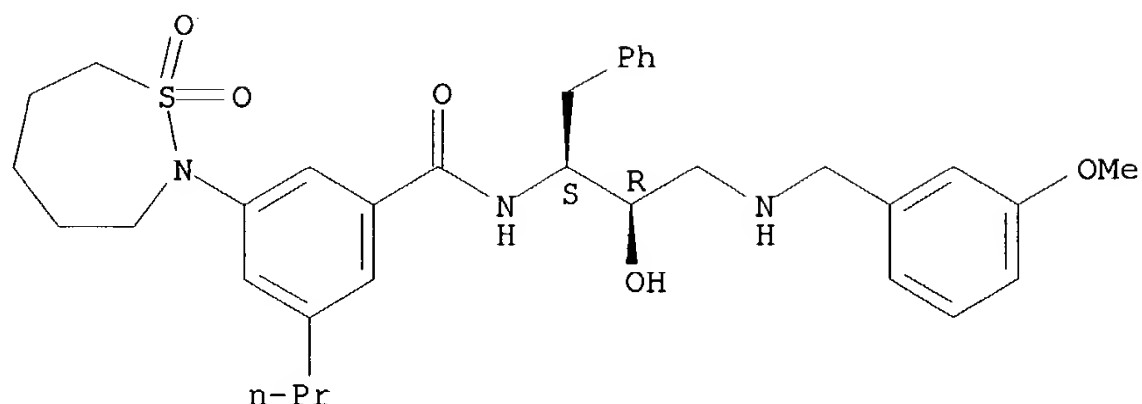
Absolute stereochemistry.



RN 706793-31-9 CAPLUS

CN Benzamide, N-[(1S,2R)-2-hydroxy-3-[[[3-methoxyphenyl]methyl]amino]-1-(phenylmethyl)propyl]-3-propyl-5-(tetrahydro-1,1-dioxido-1,2-thiazepin-2(3H)-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **706795-62-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]-3-(2-oxopyrrolidin-1-yl)-5-((E)-styryl)benzamide **706795-63-3P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]-3-(2-oxopyrrolidin-1-yl)-5-phenethylbenzamide **706795-64-4P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]-3-cyclopentyl-5-(2-oxopyrrolidin-1-yl)benzamide **706795-67-7P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]-3-cyclohexyl-5-(2-oxopyrrolidin-1-yl)benzamide **706795-68-8P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]-3-(2-oxopyrrolidin-1-yl)-5-propylbenzamide **706795-69-9P**, N-(1-Benzyl-3-cyclohexylamino-2-hydroxypropyl)-3-(2-oxopyrrolidin-1-yl)-5-propylbenzamide **706795-70-2P**, N-[1-Benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]-3-(2-methylpropenyl)-5-(2-oxopyrrolidin-1-yl)benzamide **706795-71-3P**, N-[1-Benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]-3-isobutyl-5-(2-oxopyrrolidin-1-yl)benzamide **706795-72-4P**, N-(1-Benzyl-3-cyclohexylamino-2-hydroxypropyl)-3-isopropyl-5-(2-oxopyrrolidin-1-yl)benzamide **706795-73-5P**, N-(1-Benzyl-3-cyclohexylamino-2-hydroxypropyl)-3-isobutyl-5-(2-oxopyrrolidin-1-yl)benzamide **706795-74-6P**, N-(1-Benzyl-3-cyclohexylamino-2-hydroxypropyl)-3-cyclopentyl-5-(2-oxopyrrolidin-1-yl)benzamide **706795-75-7P**, N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-cyclopentyl-5-(2-oxopyrrolidin-1-yl)benzamide **706795-76-8P**, N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-(2-oxopyrrolidin-1-yl)-5-propylbenzamide **706795-79-1P**, N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-ethynyl-5-(2-oxopyrrolidin-1-yl)benzamide **706795-82-6P**, N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-2-fluoro-3-(2-oxopyrrolidin-1-yl)-5-trifluoromethylbenzamide formate **706795-84-8P**, 5-Cyclopentyl-3-(1,1-dioxotetrahydro-2H-1,2-thiazin-2-yl)-2-fluoro-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)phenyl]methyl]amino]propyl]benzamide formate **706795-88-2P**, 5-Cyclopentyl-3-(1,1-dioxotetrahydro-2H-1,2-thiazin-2-yl)-N-[(1S,2R)-3-[[[1-ethyl-1H-pyrazol-4-yl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-2-fluorobenzamide formate **706795-90-6P**, 3-(1,1-Dioxotetrahydro-2H-1,2-thiazin-2-yl)-2-fluoro-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)phenyl]methyl]amino]propyl]-5-[(1-methylethyl)amino]benzamide formate **706795-96-2P**, 3-(1,1-Dioxotetrahydro-2H-1,2-thiazin-2-yl)-N-[(1S,2R)-3-[[[1-ethyl-1H-pyrazol-4-yl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-2-fluoro-5-[(1-methylethyl)amino]benzamide formate **706796-02-3P**, 3-(1,1-Dioxotetrahydro-2H-1,2-thiazin-2-yl)-2-fluoro-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-(tetrahydro-2H-pyran-4-ylamino)propyl]-5-[(1-methylethyl)amino]benzamide formate **706796-33-0P**, N-[(1S,2R)-1-Benzyl-3-cyclopropylamino-2-hydroxypropyl]-3-ethylamino-5-(2-

oxopyrrolidin-1-yl)benzamide **706796-35-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]-3-ethylamino-5-(2-oxopyrrolidin-1-yl)benzamide formate **706796-36-3P**, N-[(1S,2R)-1-Benzyl-3-cyclohexylamino-2-hydroxypropyl]-3-ethylamino-5-(2-oxopyrrolidin-1-yl)benzamide **706796-37-4P**, N-[(1S,2R)-1-Benzyl-3-cyclohexylamino-2-hydroxypropyl]-3-ethylamino-5-(2-oxopyrrolidin-1-yl)benzamide formate **706796-40-9P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(4-methoxybenzylamino)propyl]-3-ethylamino-5-(2-oxopyrrolidin-1-yl)benzamide **706796-42-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-ethylamino-5-(2-oxopyrrolidin-1-yl)benzamide **706796-47-6P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(2-methoxybenzylamino)propyl]-3-ethylamino-5-(2-oxopyrrolidin-1-yl)benzamide **706796-48-7P**, N-[(1S,2R)-1-Benzyl-3-[[3,5-bis(trifluoromethyl)benzyl]amino]-2-hydroxypropyl]-3-ethylamino-5-(2-oxopyrrolidin-1-yl)benzamide **706796-55-6P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(3-trifluoromethoxybenzylamino)propyl]-3-ethylamino-5-(2-oxopyrrolidin-1-yl)benzamide **706796-62-5P**, N-[(1S,2R)-1-Benzyl-3-cyclopentylamino-2-hydroxypropyl]-3-ethylamino-5-(2-oxopyrrolidin-1-yl)benzamide **706796-67-0P**, N-(1-Benzyl-3-cyclobutylamino-2-hydroxypropyl)-3-ethylamino-5-(2-oxopyrrolidin-1-yl)benzamide **706796-68-1P**, N-(1-Benzyl-3-cycloheptylamino-2-hydroxypropyl)-3-ethylamino-5-(2-oxopyrrolidin-1-yl)benzamide **706796-84-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]-3-isopropoxy-5-(2-oxopyrrolidin-1-yl)benzamide **706796-88-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]-3-(2-oxopyrrolidin-1-yl)-5-pentoxybenzamide **706796-89-6P**, N-[(1S,2R)-1-Benzyl-3-benzylamino-2-hydroxypropyl]-3-(2-oxopyrrolidin-1-yl)-5-pentoxybenzamide **706796-91-0P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(phenethylamino)propyl]-3-(2-oxopyrrolidin-1-yl)-5-pentoxybenzamide **706796-93-2P**, N-[(1S,2R)-1-Benzyl-3-cyclohexylamino-2-hydroxypropyl]-3-(2-oxopyrrolidin-1-yl)-5-pentoxybenzamide **706796-94-3P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(1-methylpiperidin-4-ylamino)propyl]-3-(2-oxopyrrolidin-1-yl)-5-pentoxybenzamide **706796-98-7P**, N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-ethoxy-5-(2-oxopyrrolidin-1-yl)benzamide **706797-01-5P**, N-(1-Benzyl-3-cyclohexylamino-2-hydroxypropyl)-3-ethoxy-5-(2-oxopyrrolidin-1-yl)benzamide **706797-02-6P**, N-[1-Benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]-3-ethoxy-5-(2-oxopyrrolidin-1-yl)benzamide **706797-04-8P**, N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-(methylsulfonyl)-5-(2-oxopyrrolidin-1-yl)benzamide **706797-06-0P**, N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-(ethylsulfonyl)-5-(2-oxopyrrolidin-1-yl)benzamide **706797-08-2P**, N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-ethanesulfonyl-5-(2-oxopyrrolidin-1-yl)benzamide **706797-10-6P**, N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-(methanesulfonyl)-5-(2-oxopyrrolidin-1-yl)benzamide **706797-33-3P**, N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-propylbenzamide **706797-36-6P**, N-(1-Benzyl-3-cyclohexylamino-2-hydroxypropyl)-3-(1,1-dioxoisothiazolidin-2-yl)-5-propylbenzamide **706797-37-7P**, N-[1-Benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-propylbenzamide **706797-40-2P**, N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-cyano-5-(1,1-dioxoisothiazolidin-2-yl)benzamide **706797-42-4P**, N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-ethynylbenzamide formate **706797-66-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-ethylaminobenzamide formate **706797-68-4P**, N-[(1S,2R)-1-Benzyl-2-

hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-ethylaminobenzamide formate **706797-69-5P**,
N-((1S,2R)-1-Benzyl-3-cyclohexylamino-2-hydroxypropyl)-3-(1,1-dioxoisothiazolidin-2-yl)-5-ethylaminobenzamide **706797-71-9P**,
N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-(morpholin-4-yl)benzamide formate **706797-73-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-(pyrrolidin-1-yl)benzamide formate **706797-75-3P**,
N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-methylaminobenzamide formate **706797-77-5P**, N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-ethoxybenzamide **706797-80-0P**, N-[1-Benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-ethoxybenzamide **706797-81-1P**, N-(1-Benzyl-3-cyclohexylamino-2-hydroxypropyl)-3-(1,1-dioxoisothiazolidin-2-yl)-5-ethoxybenzamide **706797-86-6P**, N-(1-Benzyl-3-cyclopropylamino-2-hydroxypropyl)-3-(1,1-dioxoisothiazolidin-2-yl)-5-ethoxybenzamide **706797-87-7P**,
N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethoxybenzylamino)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-ethoxybenzamide **706797-88-8P**,
N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-(methylsulfonyl)benzamide **706797-89-9P**,
N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-(ethylsulfonyl)benzamide **706797-90-2P**,
N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-(ethanesulfonyl)benzamide **706797-91-3P**,
N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-(Methanesulfonyl)benzamide **706797-94-6P**, 3-(1,1-Dioxotetrahydro-2H-1,2-thiazin-2-yl)-2-fluoro-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-[(trifluoromethyl)oxy]phenyl]methyl]amino]propyl]-5-[(1-methylethyl)amino]benzamide formate **706797-95-7P**, 3-(1,1-Dioxotetrahydro-2H-1,2-thiazin-2-yl)-5-(ethylamino)-N-[(1S,2R)-3-[[[3-ethyl-5-isoxazolyl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-2-fluorobenzamide **706797-96-8P**,
4-(1,1-Dioxotetrahydro-2H-1,2-thiazin-2-yl)-1-ethyl-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-(tetrahydro-2H-pyran-4-ylamino)propyl]-1H-benzimidazole-6-carboxamide **706797-97-9P**, 8-(1,1-Dioxoisothiazolidin-2-yl)-4-ethyl-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-(tetrahydro-2H-pyran-4-ylamino)propyl]-1,2,3,4-tetrahydro-6-quinoxalinecarboxamide **706797-98-0P**, 8-(1,1-Dioxoisothiazolidin-2-yl)-4-ethyl-N-[(1S,2R)-3-[[[1-ethyl-1H-pyrazol-4-yl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-1,2,3,4-tetrahydro-6-quinoxalinecarboxamide **706798-02-9P**, N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-5-(1,1-dioxo-1,2-thiazinan-2-yl)-N',N'-dipropylisophthalamide **706798-03-0P**, N-(1-Benzyl-3-cyclopropylamino-2-hydroxypropyl)-5-(1,1-dioxo-1,2-thiazinan-2-yl)-N',N'-dipropylisophthalamide **706798-04-1P**, N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-propylbenzamide **706798-06-3P**, N-[1-Benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-propylbenzamide formate **706798-10-9P**, N-[1-Benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]-5-(1,1-dioxo-1,2-thiazinan-2-yl)-N',N'-dipropylisophthalamide **706798-12-1P**, N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethoxybenzylamino)propyl]-5-(1,1-dioxo-1,2-thiazinan-2-yl)-N',N'-dipropylisophthalamide formate **706798-14-3P**,
N-[1-Benzyl-2-hydroxy-3-(3-trifluoromethylbenzylamino)propyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-ethylaminobenzamide formate **706798-17-6P**,
N-[1-Benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-ethylaminobenzamide formate **706798-22-3P**,

N-[(1S,2R)-1-Benzyl-3-[(3,5-dichlorobenzyl)amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate
706798-24-5P, N-[(1S,2R)-1-Benzyl-3-[(2-fluoro-5-methoxybenzyl)amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-26-7P**, N-[(1S,2R)-1-Benzyl-3-[(4-fluoro-3-methoxybenzyl)amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-28-9P**,
 N-[(1S,2R)-1-Benzyl-3-[(3,5-dimethylbenzyl)amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate
706798-29-0P, N-[(1S,2R)-1-Benzyl-3-[(3,5-difluorobenzyl)amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide
706798-30-3P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[3-nitro-5-(trifluoromethyl)benzyl]amino]propyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide **706798-31-4P**, N-[(1S,2R)-1-Benzyl-3-[[5-cyanopyridin-3-yl)methyl]amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide **706798-33-6P**,
 N-[(1S,2R)-1-Benzyl-3-[(3-chloro-5-methoxybenzyl)amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate
706798-34-7P, N-[(1S,2R)-1-Benzyl-3-[(3-bromo-5-fluorobenzyl)amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide **706798-35-8P**, 5-[[[(2R,3S)-3-[[3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzoyl]amino]-2-hydroxy-4-phenylbutyl]amino]methyl]-N-methylnicotinamide **706798-37-0P**,
 N-[(1S,2R)-1-Benzyl-3-[(3-bromo-5-methoxybenzyl)amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate
706798-38-1P 706798-39-2P, N-[(1S,2R)-1-Benzyl-3-[(3,5-di-tert-butylbenzyl)amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide **706798-41-6P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[3-methyl-5-(methylsulfonyl)benzyl]amino]propyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide **706798-43-8P**,
 N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxy-5-methylbenzyl)amino]propyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide
706798-45-0P, Dimethyl 5-[[[(2R,3S)-3-[[3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzoyl]amino]-2-hydroxy-4-phenylbutyl]amino]methyl]isophthalate **706798-47-2P**,
 N-[(1S,2R)-1-Benzyl-3-[(3,5-diisopropoxybenzyl)amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide
706798-48-3P, N-[(1S,2R)-1-Benzyl-3-[[4-bromo-2-thienyl)methyl]amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide **706798-49-4P**, N-[(1S,2R)-1-Benzyl-3-[(2,3-dihydro-1-benzofuran-6-yl)methyl]amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide **706798-51-8P**,
 N-[(1S,2R)-1-Benzyl-3-[[4-chloro-1-methyl-1H-pyrazol-3-yl)methyl]amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-52-9P**, N-[(1S,2R)-1-Benzyl-3-[[2-bromo-1,3-thiazol-5-yl)methyl]amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide **706798-53-0P**, N-[(1S,2R)-1-Benzyl-3-[[4-bromo-1H-pyrrol-2-yl)methyl]amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide **706798-55-2P**,
 N-[(1S,2R)-1-Benzyl-3-[[2-butyl-1H-imidazol-4-yl)methyl]amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-56-3P**, N-[(1S,2R)-1-Benzyl-3-[(3-bromobenzyl)amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide **706798-57-4P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-nitrobenzyl)amino]propyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide **706798-58-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-thienylmethyl)amino]propyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide **706798-59-6P**, N-[(1S,2R)-1-Benzyl-3-[[4-bromo-1-methyl-1H-pyrazol-3-yl)methyl]amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide **706798-60-9P**,

N-[(1S,2R)-1-Benzyl-3-[[3-fluoro-5-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide
706798-62-1P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-vinylbenzyl)amino]propyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-64-3P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[4-methoxy-3-thienyl)methyl]amino]propyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-66-5P**, 3-[[[(2R,3S)-3-[[3-(1,1-Dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzoyl]amino]-2-hydroxy-4-phenylbutyl]amino]methyl]benzoic acid formate **706798-69-8P**, N-[(1S,2R)-1-Benzyl-3-[(3,4-dimethoxybenzyl)amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-71-2P**, N-[(1S,2R)-1-Benzyl-3-[[5-ethyl-2-furyl)methyl]amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-73-4P**, N-[(1S,2R)-1-Benzyl-3-[(2,3-dihydro-1,4-benzodioxin-6-yl)methyl]amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-75-6P**, N-[(1S,2R)-1-Benzyl-3-[(3-ethoxy-4-methoxybenzyl)amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-77-8P**, N-[(1S,2R)-1-Benzyl-3-[[5-ethyl-2-thienyl)methyl]amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-79-0P**, N-[(1S,2R)-1-Benzyl-3-[(3-chloro-4-fluorobenzyl)amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-80-3P**, 3-(1,1-Dioxotetrahydro-2H-1,2-thiazin-2-yl)-5-(ethylamino)-N-[(1S,2R)-3-[[1-ethyl-1H-pyrazol-4-yl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]benzamide **706798-81-4P**, N-[(1S,2R)-1-Benzyl-3-[[1-ethyl-1H-pyrazol-4-yl)methyl]amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-83-6P**, N-[(1S,2R)-1-Benzyl-3-[[1-ethyl-3-methyl-1H-pyrazol-4-yl)methyl]amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-85-8P**, N-[(1S,2R)-1-Benzyl-3-[[2,2-dimethyl-3,4-dihydro-2H-chromen-6-yl)methyl]amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-87-0P 706798-89-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[6-methylpyridin-2-yl)methyl]amino]propyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-91-6P**, N-[(1S,2R)-1-Benzyl-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-92-7P**, N-[(1S,2R)-1-Benzyl-3-[[1-ethyl-1H-pyrazol-4-yl)methyl]amino]-2-hydroxypropyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)-2-fluorobenzamide **706798-94-9P**, N-[(1S,2R)-1-Benzyl-3-[[1-ethyl-1H-pyrazol-4-yl)methyl]amino]-2-hydroxypropyl]-3-(ethylamino)-5-(2-oxopyrrolidin-1-yl)benzamide formate **706798-96-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxy-4-methylbenzyl)amino]propyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706798-98-3P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxy-2-methylbenzyl)amino]propyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(ethylamino)benzamide formate **706799-11-3P**, N-[(1S,2R)-3-[[3,5-Dibromophenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-[(1-methylethyl)oxy]-5-(2-oxo-1-pyrrolidinyl)benzamide **706799-12-4P**, N-[(1S,2R)-2-Hydroxy-1-(phenylmethyl)-3-[(phenylmethyl)amino]propyl]-3-[(1-methylethyl)oxy]-5-(2-oxo-1-pyrrolidinyl)benzamide **706799-13-5P**, N-[(1S,2R)-3-[[3-Bromophenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-[(1-methylethyl)oxy]-5-(2-oxo-1-pyrrolidinyl)benzamide **706799-14-6P**, N-[(1S,2R)-3-[[3-(Ethoxy)phenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-[(1-methylethyl)oxy]-5-(2-oxo-1-pyrrolidinyl)benzamide **706799-15-7P**, N-[(1S,2R)-3-[[3-Chlorophenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-[(1-methylethyl)oxy]-5-(2-oxo-1-

pyrrolidinyl)benzamide **706799-16-8P**, N-[(1S,2R)-2-Hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)oxy]phenyl]methyl]amino]propyl]-3-[(1-methylethyl)oxy]-5-(2-oxo-1-pyrrolidinyl)benzamide **706799-17-9P**, N-[(1S,2R)-3-[[3,5-Bis(methoxy)phenyl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-[1-methylethoxy]-5-(2-oxo-1-pyrrolidinyl)benzamide **706799-18-0P**, N-[(1S,2R)-3-[[3,5-Dichlorophenyl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-[(1-methylethyl)oxy]-5-(2-oxo-1-pyrrolidinyl)benzamide **706799-19-1P**, N-[(1S,2R)-3-[[3,5-Difluorophenyl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-[(1-methylethyl)oxy]-5-(2-oxo-1-pyrrolidinyl)benzamide **706799-20-4P**, N-[(1S,2R)-2-Hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)phenyl]methyl]amino]propyl]-3-[(1-methylethyl)oxy]-5-(2-oxo-1-pyrrolidinyl)benzamide **706799-22-6P**, N-[(1S,2R)-3-[[[3,5-Bis(trifluoromethyl)phenyl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-[(1-methylethyl)oxy]-5-(2-oxo-1-pyrrolidinyl)benzamide **706799-24-8P**, N-[(1S,2R)-2-Hydroxy-3-[[[3-methylphenyl]methyl]amino]-1-(phenylmethyl)propyl]-3-[(1-methylethyl)oxy]-5-(2-oxo-1-pyrrolidinyl)benzamide **706799-26-0P**, 3-(1,1-Dioxotetrahydro-2H-1,2-thiazin-2-yl)-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)phenyl]methyl]amino]propyl]-5-[(1-methylethyl)oxy]benzamide hydrochloride **706799-27-1P**, 3-(1,1-Dioxotetrahydro-2H-1,2-thiazin-2-yl)-N-[(1S,2R)-2-hydroxy-3-[[[3-methoxyphenyl]methyl]amino]-1-(phenylmethyl)propyl]-5-[(1-methylethyl)oxy]benzamide hydrochloride **706799-29-3P**, 3-(1,1-Dioxotetrahydro-2H-1,2-thiazin-2-yl)-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)oxy]phenyl]methyl]amino]propyl]-5-[(1-methylethyl)oxy]benzamide hydrochloride **706799-31-7P**, N-[(1S,2R)-3-[[[3,5-Bis(trifluoromethyl)phenyl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(1,1-dioxotetrahydro-2H-1,2-thiazin-2-yl)-5-[(1-methylethyl)oxy]benzamide hydrochloride **706799-33-9P**, N-[(1S,2R)-3-[[[3,5-Bis(methoxy)phenyl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(1,1-dioxotetrahydro-2H-1,2-thiazin-2-yl)-5-[1-methylethoxy]benzamide hydrochloride **706799-35-1P**, N-[(1S,2R)-3-[[[3,5-Dibromophenyl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(1,1-dioxotetrahydro-2H-1,2-thiazin-2-yl)-5-[(1-methylethyl)oxy]benzamide hydrochloride **706799-37-3P**, 3-Cyclopentyl-5-(1,1-dioxotetrahydro-2H-1,2-thiazin-2-yl)-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)phenyl]methyl]amino]propyl]benzamide hydrochloride **706799-39-5P**, 3-Cyclopentyl-5-(1,1-dioxotetrahydro-2H-1,2-thiazin-2-yl)-N-[(1S,2R)-2-hydroxy-3-[[[3-methoxyphenyl]methyl]amino]-1-(phenylmethyl)propyl]benzamide hydrochloride **706799-41-9P**, 3-Cyclopentyl-5-(1,1-dioxotetrahydro-2H-1,2-thiazin-2-yl)-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)oxy]phenyl]methyl]amino]propyl]benzamide hydrochloride **706799-43-1P**, N-[(1S,2R)-3-[[[3,5-Bis(trifluoromethyl)phenyl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-cyclopentyl-5-(1,1-dioxotetrahydro-2H-1,2-thiazin-2-yl)benzamide hydrochloride **706799-45-3P**, N-[(1S,2R)-3-[[[3,5-Bis(methoxy)phenyl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-cyclopentyl-5-(1,1-dioxotetrahydro-2H-1,2-thiazin-2-yl)benzamide hydrochloride **706799-46-4P**, 3-Cyclopentyl-N-[(1S,2R)-3-[[[3,5-dibromophenyl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-5-(1,1-dioxotetrahydro-2H-1,2-thiazin-2-yl)benzamide hydrochloride **706799-47-5P**, 3-(1,1-Dioxotetrahydro-2H-1,2-thiazin-2-yl)-5-(ethylamino)-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)oxy]phenyl]methyl]amino]propyl]benzamide hydrochloride **706799-49-7P**, N-[(1S,2R)-3-[[[3,5-Bis(trifluoromethyl)phenyl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(1,1-dioxotetrahydro-2H-1,2-thiazin-2-yl)-5-(ethylamino)benzamide hydrochloride **706799-50-0P**, N-[(1S,2R)-3-[[[3,5-Bis(methoxy)phenyl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(1,1-dioxotetrahydro-2H-1,2-thiazin-2-yl)-5-

(ethylamino)benzamide hydrochloride **706799-52-2P**,
N-[(1S,2R)-3-[[[3,5-Dibromophenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(1,1-dioxotetrahydro-2H-1,2-thiazin-2-yl)-5-(ethylamino)benzamide hydrochloride **706799-53-3P**,
3-(Ethoxy)-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)oxy]phenyl)methyl]amino]propyl]-5-(2-oxo-1-pyrrolidinyl)benzamide hydrochloride **706799-55-5P**,
N-[(1S,2R)-3-[[[3,5-Bis(trifluoromethyl)phenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(ethoxy)-5-(2-oxo-1-pyrrolidinyl)benzamide hydrochloride **706799-56-6P**, N-[(1S,2R)-3-[[[3,5-Bis(methoxy)phenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(ethoxy)-5-(2-oxo-1-pyrrolidinyl)benzamide hydrochloride **706799-58-8P**, N-[(1S,2R)-3-[[[3,5-Dibromophenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(ethoxy)-5-(2-oxo-1-pyrrolidinyl)benzamide hydrochloride **706799-60-2P**,
3-Cyclopentyl-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)oxy]phenyl)methyl]amino]propyl]-5-(2-oxo-1-pyrrolidinyl)benzamide hydrochloride **706799-62-4P**,
N-[(1S,2R)-3-[[[3,5-Bis(trifluoromethyl)phenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-cyclopentyl-5-(2-oxo-1-pyrrolidinyl)benzamide hydrochloride **706799-64-6P**, N-[(1S,2R)-3-[[[3,5-Bis(methoxy)phenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-cyclopentyl-5-(2-oxo-1-pyrrolidinyl)benzamide hydrochloride **706799-66-8P**, 3-Cyclopentyl-N-[(1S,2R)-3-[[[3,5-dibromophenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-5-(2-oxo-1-pyrrolidinyl)benzamide hydrochloride **706799-68-0P**,
N-[(1S,2R)-3-[[[3,5-Bis(methoxy)phenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(ethylamino)-5-(2-oxo-1-pyrrolidinyl)benzamide hydrochloride **706799-70-4P**, N-[(1S,2R)-3-[[[3,5-Dibromophenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(ethylamino)-5-(2-oxo-1-pyrrolidinyl)benzamide hydrochloride **706799-72-6P**, N-[(1S,2R)-3-[[[3,5-Bis(trifluoromethyl)phenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-(ethoxy)benzamide hydrochloride **706799-74-8P**,
N-[(1S,2R)-3-[[[3,5-Bis(methoxy)phenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-(ethoxy)benzamide hydrochloride **706799-76-0P**, N-[(1S,2R)-3-[[[3,5-Dibromophenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-(ethoxy)benzamide hydrochloride **706799-78-2P**, 3-(1,1-Dioxoisothiazolidin-2-yl)-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)phenyl)methyl]amino]propyl]-5-[(1-methylethyl)oxy]benzamide hydrochloride **706799-80-6P**,
3-(1,1-Dioxoisothiazolidin-2-yl)-N-[(1S,2R)-2-hydroxy-3-[[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-5-[(1-methylethyl)oxy]benzamide hydrochloride **706799-82-8P**,
3-(1,1-Dioxoisothiazolidin-2-yl)-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-[(trifluoromethyl)oxy]phenyl)methyl]amino]propyl]-5-[(1-methylethyl)oxy]benzamide hydrochloride **706799-84-0P**,
N-[(1S,2R)-3-[[[3,5-Bis(trifluoromethyl)phenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-[(1-methylethyl)oxy]benzamide hydrochloride **706799-86-2P**,
N-[(1S,2R)-3-[[[3,5-Dibromophenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(1,1-dioxoisothiazolidin-2-yl)-5-[(1-methylethyl)oxy]benzamide hydrochloride **706799-88-4P**,
3-Cyclopentyl-5-(1,1-dioxoisothiazolidin-2-yl)-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-(trifluoromethyl)phenyl)methyl]amino]propyl]benzamide hydrochloride **706799-89-5P**, 3-Cyclopentyl-5-(1,1-dioxoisothiazolidin-2-yl)-N-[(1S,2R)-2-hydroxy-3-[[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]benzamide hydrochloride **706799-91-9P**, 3-Cyclopentyl-5-(1,1-dioxoisothiazolidin-2-yl)-N-

09/895,871

[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[3-[(trifluoromethyl)oxy]phenyl]methyl]amino]propyl]benzamide hydrochloride **706799-93-1P**,
N-[(1S,2R)-3-[[[3,5-Bis(trifluoromethyl)phenyl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-cyclopentyl-5-(1,1-dioxoisothiazolidin-2-yl)benzamide hydrochloride

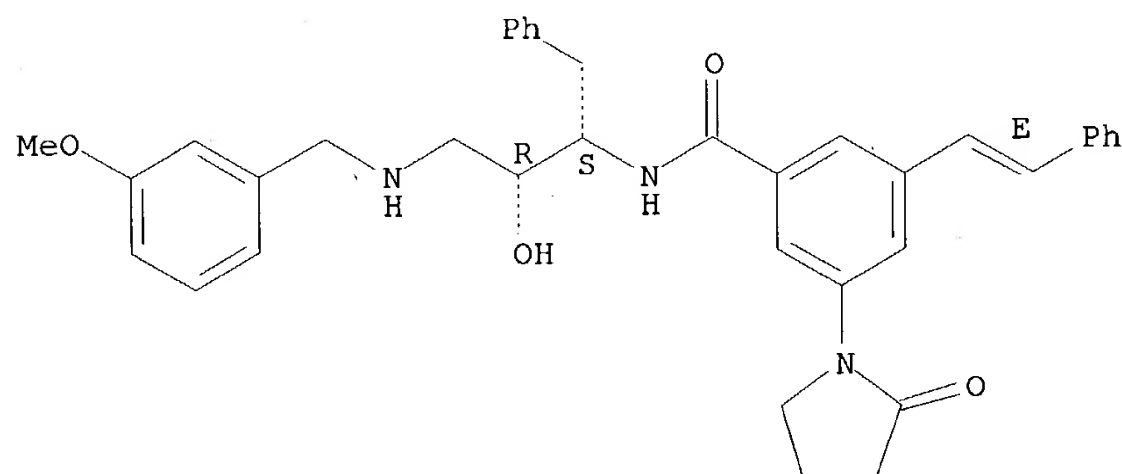
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of hydroxyethylamine derivs. for treatment of Alzheimer's disease)

RN 706795-62-2 CAPLUS

CN Benzamide, N-[(1R,2S)-2-hydroxy-3-[[[3-methoxyphenyl]methyl]amino]-1-(phenylmethyl)propyl]-3-(2-oxo-1-pyrrolidinyl)-5-[(1E)-2-phenylethenyl]-, rel- (9CI) (CA INDEX NAME)

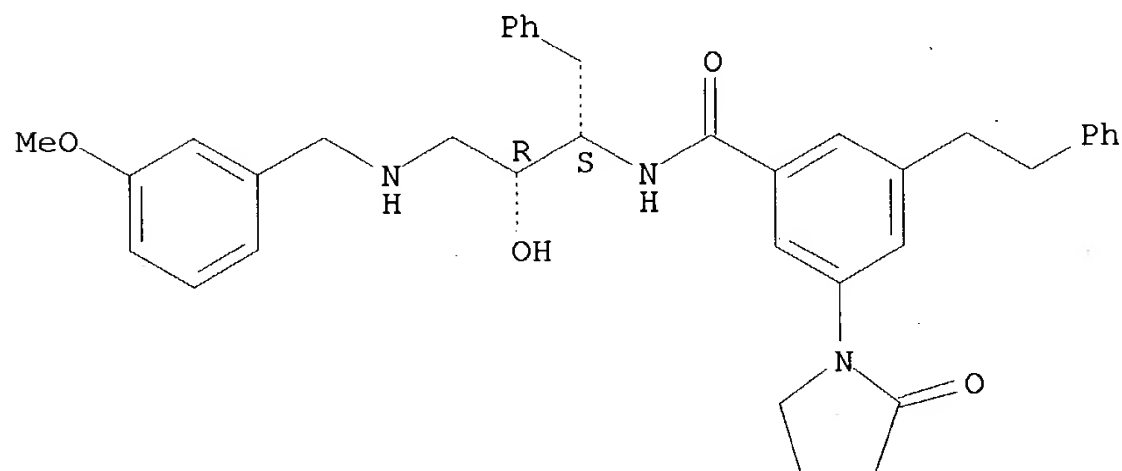
Relative stereochemistry.
Double bond geometry as shown.



RN 706795-63-3 CAPLUS

CN Benzamide, N-[(1S,2R)-2-hydroxy-3-[[[3-methoxyphenyl]methyl]amino]-1-(phenylmethyl)propyl]-3-(2-oxo-1-pyrrolidinyl)-5-(2-phenylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

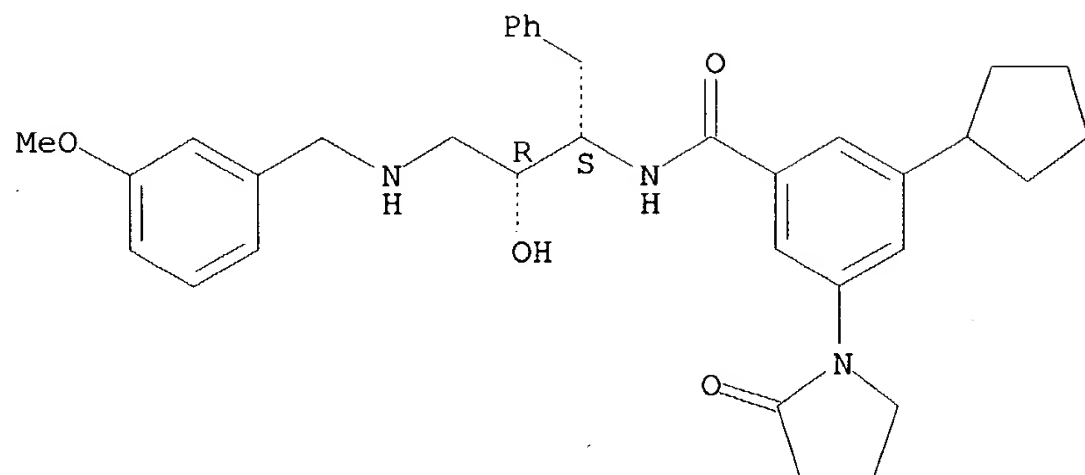


RN 706795-64-4 CAPLUS

CN Benzamide, 3-cyclopentyl-N-[(1S,2R)-2-hydroxy-3-[[[3-methoxyphenyl]methyl]amino]-1-(phenylmethyl)propyl]-5-(2-oxo-1-pyrrolidinyl)- (9CI) (CA INDEX NAME)

09/895,871

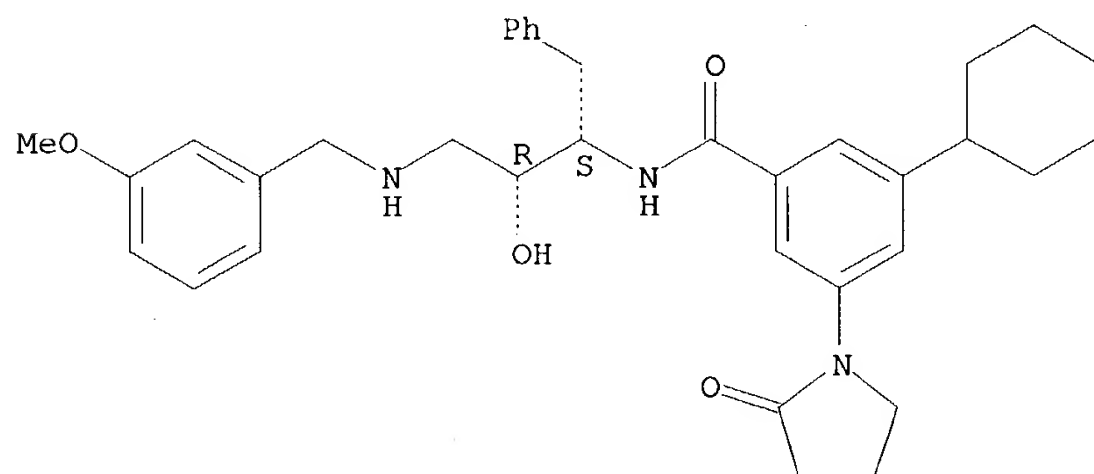
Absolute stereochemistry.



RN 706795-67-7 CAPLUS

CN Benzamide, 3-cyclohexyl-N-[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-5-(2-oxo-1-pyrrolidinyl)- (9CI) (CA INDEX NAME)

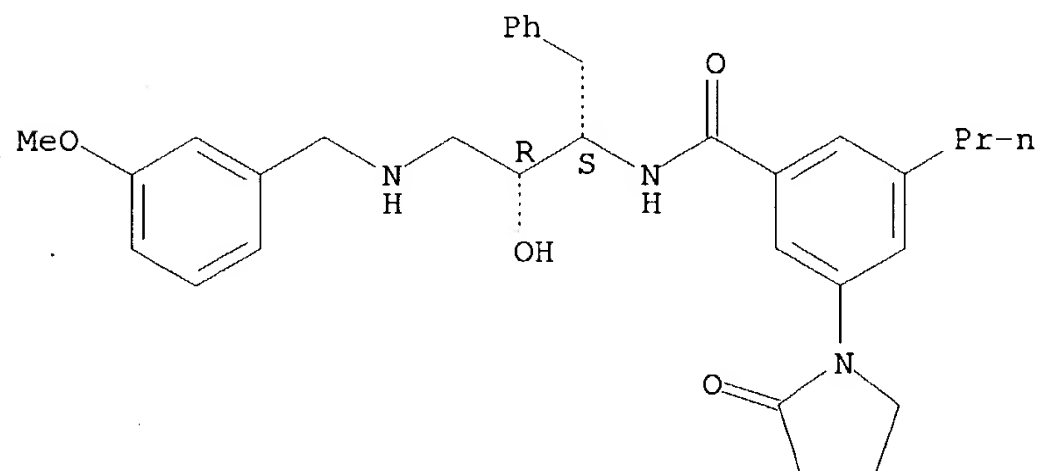
Absolute stereochemistry.



RN 706795-68-8 CAPLUS

CN Benzamide, N-[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-3-(2-oxo-1-pyrrolidinyl)-5-propyl- (9CI) (CA INDEX NAME)

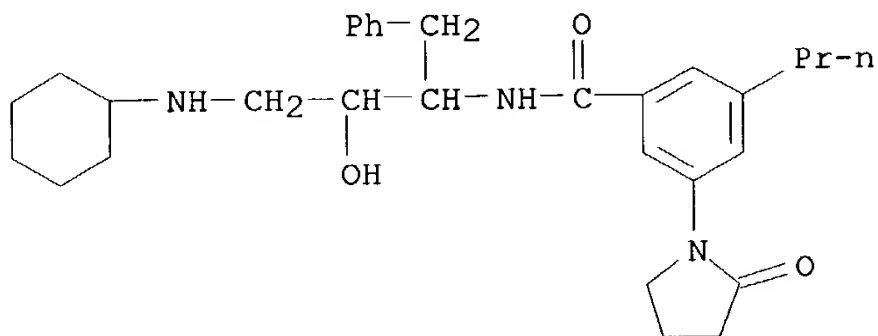
Absolute stereochemistry.



09/895,871

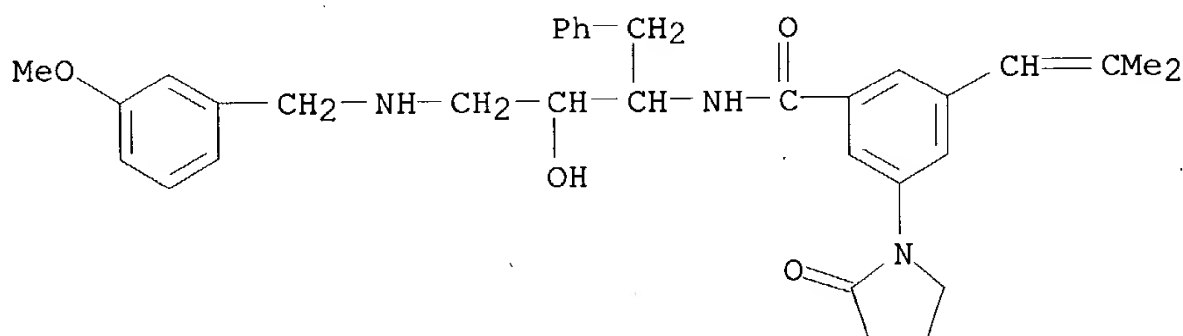
RN 706795-69-9 CAPLUS

CN Benzamide, N-[3-(cyclohexylamino)-2-hydroxy-1-(phenylmethyl)propyl]-3-(2-oxo-1-pyrrolidinyl)-5-propyl- (9CI) (CA INDEX NAME)



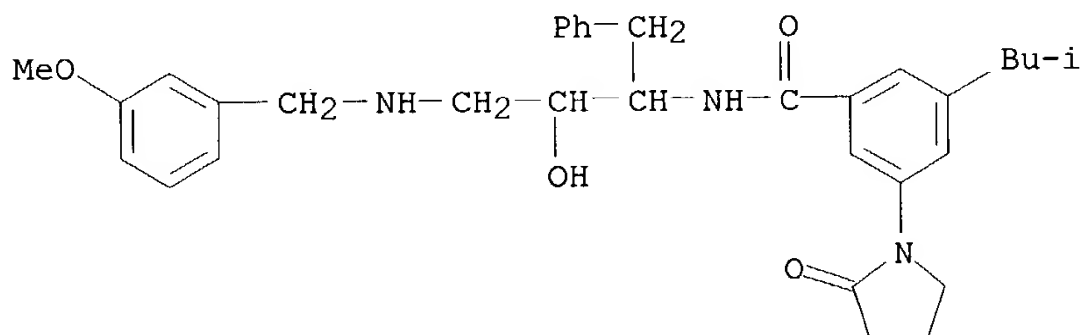
RN 706795-70-2 CAPLUS

CN Benzamide, N-[2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-3-(2-methyl-1-propenyl)-5-(2-oxo-1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



RN 706795-71-3 CAPLUS

CN Benzamide, N-[2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-3-(2-methylpropyl)-5-(2-oxo-1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



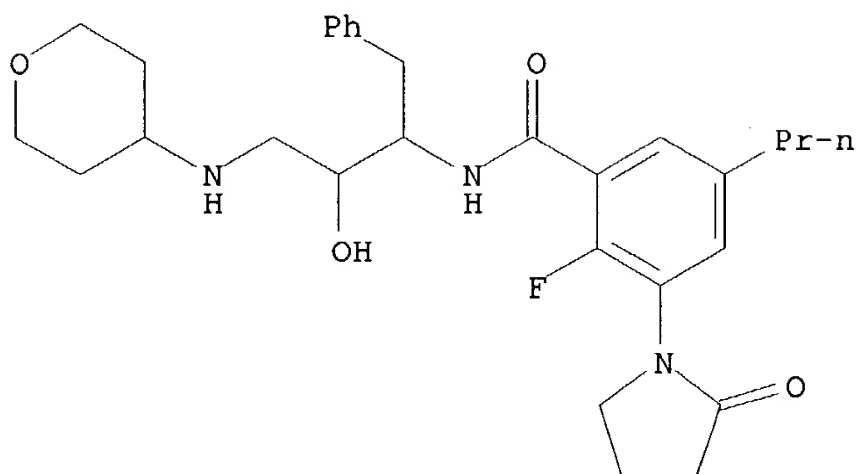
RN 706795-72-4 CAPLUS

CN Benzamide, N-[3-(cyclohexylamino)-2-hydroxy-1-(phenylmethyl)propyl]-3-(1-methylethyl)-5-(2-oxo-1-pyrrolidinyl)- (9CI) (CA INDEX NAME)

09/895,871

NAME)

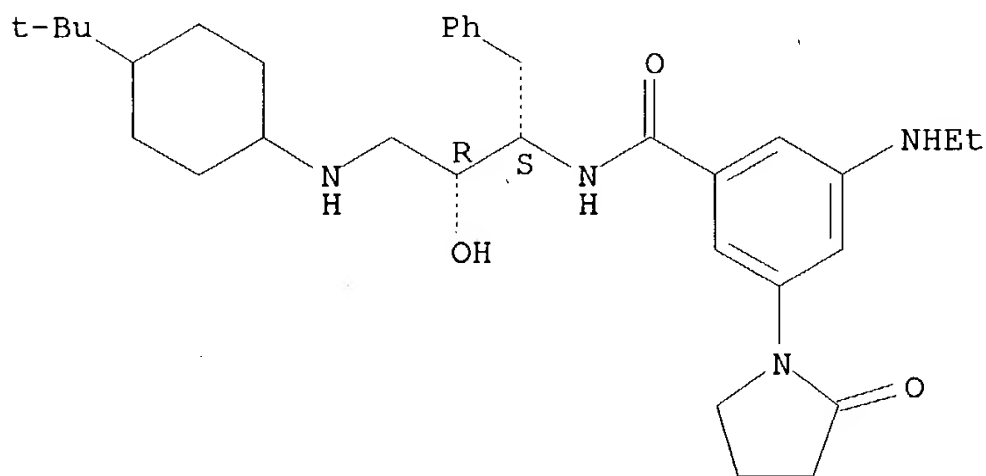
Absolute stereochemistry.



RN 708270-81-9 CAPLUS

CN Benzamide, N-[(1S,2R)-3-[[4-(1,1-dimethylethyl)cyclohexyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(ethylamino)-5-(2-oxo-1-pyrrolidinyl)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:428903 CAPLUS

DOCUMENT NUMBER: 141:6920

TITLE: Preparation of phenylcarboxamide derivatives as β -secretase inhibitors for the treatment of Alzheimer's disease

INVENTOR(S): Coburn, Craig A.; Stachel, Shawn J.; Vacca, Joseph P.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
------------	------	------	-----------------	------

WO 2004043916	A1	20040527	WO 2003-US35316	20031106
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.:

US 2002-425555P P 20021112
US 2002-425560P P 20021112

OTHER SOURCE(S): MARPAT 141:6920

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. I [R2 = R4-S(O)m-NR5-, R4-S(O)m-, R4NHCO-, R4CONH-, R4R5N-, CN, halo, etc.; R4, R5 = H, C1-C6alkyl, Ph or benzyl; R6a, R6b, R6c = H, halo, -OR5, -SR5 or C1-C6alkyl; X1 = H; X2 = OH, or X1, X2 = oxo; Z = CO, CH-OH, CH-F, or ethylene ketal; n = 1-4; m = 0-2] were prepared as β -secretase inhibitors for the treatment or prevention of diseases, such as Alzheimer's disease. For example, compound II was prepared from di-Me 5-aminoisophthalate in a multi-step synthesis. The compds. of the invention exhibited inhibiting activity against β -secretase with an IC50 from about 1nM to 1 μ M.

IT 695216-22-9P 695216-28-5P 695216-35-4P
695216-41-2P 695216-47-8P

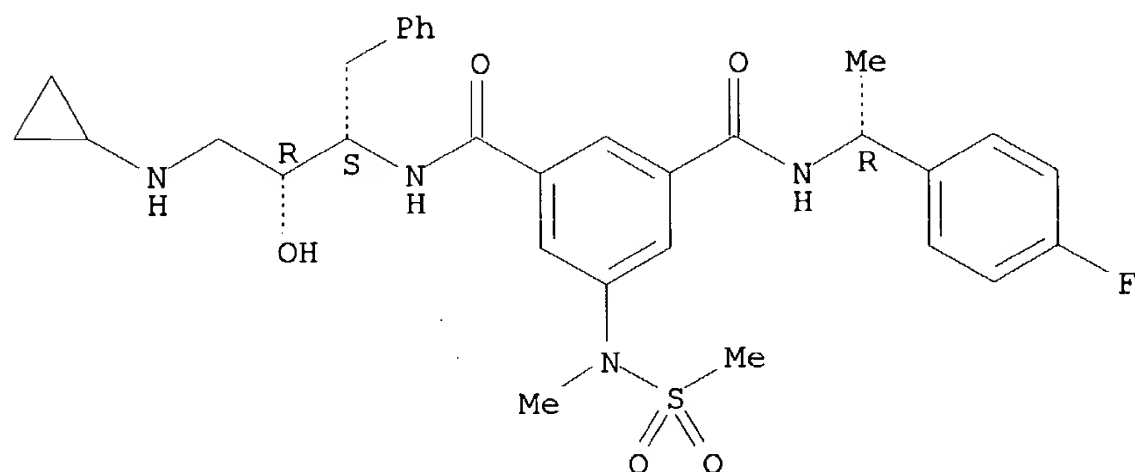
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of phenylcarboxamide derivs. as β -secretase inhibitors for the treatment of Alzheimer's disease)

RN 695216-22-9 CAPLUS

RN	895216 22 9 CARLOS
CN	1,3-Benzenedicarboxamide, N-[(1S,2R)-3-(cyclopropylamino)-2-hydroxy-1-(phenylmethyl)propyl]-N'-[(1R)-1-(4-fluorophenyl)ethyl]-5-[methyl(methylsulfonyl)amino]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

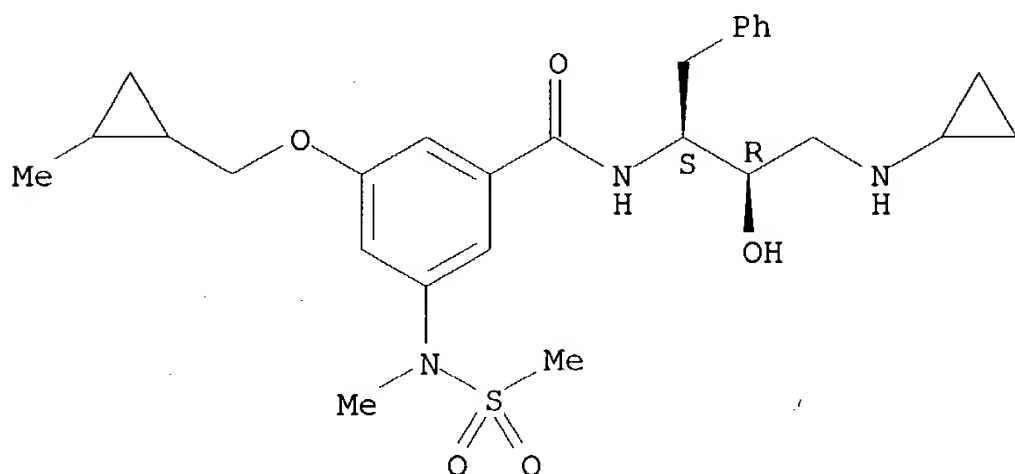


RN 695216-28-5 CAPLUS

09/895,871

CN Benzamide, N-[(1S,2R)-3-(cyclopropylamino)-2-hydroxy-1-(phenylmethyl)propyl]-3-[(2-methylcyclopropyl)methoxy]-5-[methyl(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)

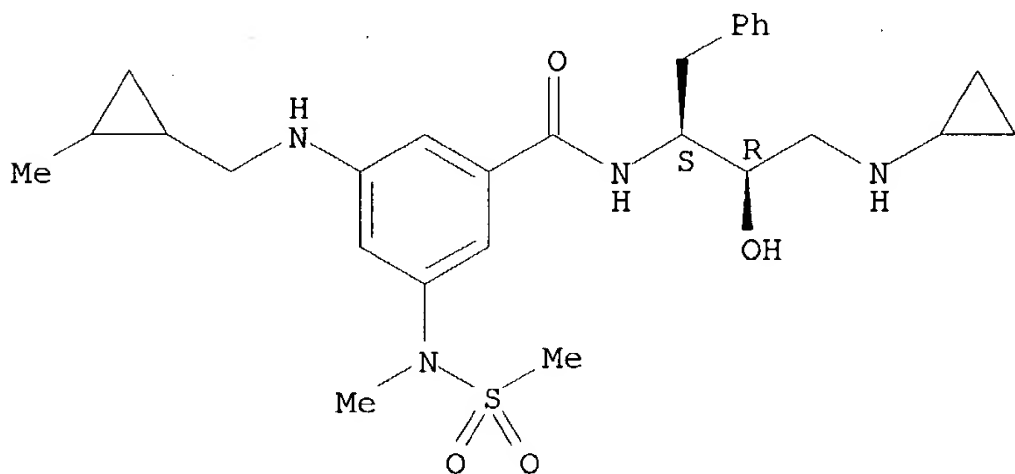
Absolute stereochemistry.



RN 695216-35-4 CAPLUS

CN Benzamide, N-[(1S,2R)-3-(cyclopropylamino)-2-hydroxy-1-(phenylmethyl)propyl]-3-[[(2-methylcyclopropyl)methyl]amino]-5-[methyl(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 695216-41-2 CAPLUS

CN Benzamide, 3-(1-cyanocyclopentyl)-N-[(1S,2R)-3-(cyclopropylamino)-2-hydroxy-1-(phenylmethyl)propyl]-5-[(2-methylcyclopropyl)methoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Chemical structure of compound 10: A cyclohexane ring substituted with a 2-methylpropyl group, a 2-cyano-1-cyclopentyl group, and a 4-(2-((S)-1-((R)-1-hydroxy-2-phenylethyl)amino)ethylamino)phenoxy group.

CN [1,1'-Biphenyl]-3-carboxamide, 2'-cyano-N-[(1S,2R)-3-(cyclopropylamino)-2-hydroxy-1-(phenylmethyl)propyl]-5-(cyclopropylmethoxy)- (9CI) (CA INDEX NAME)

Chemical structure of compound 10: A benzene ring substituted with a cyclopropylmethoxy group, a 2-cyanophenyl group, and a 2-((S)-1-((R)-1-hydroxy-2-phenylethyl)amino)acetyl group.

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
WO 2004022523	A2	20040318	WO 2003-US28116	20030908
WO 2004022523	A3	20040910		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN				

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
 PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
 TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004214890

A1

20041028

US 2003-657567

20030908

PRIORITY APPLN. INFO.:

US 2002-408783P

P 20020906

OTHER SOURCE(S):

MARPAT 140:270550

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to diamino(hydroxy)propane derivs. of formula I [wherein: R1 = -(CH2)1-2-S(O)0-2-(C1-6 alkyl) or (un)substituted (cyclo)alkyl, alk(en/yn)yl, (hetero)aryl, etc.; R2 = H, C1-6 alkyl optionally substituted with 1-3 substituents, (CH2)0-4-(hetero)aryl, C2-6 alk(en/yn)yl, etc.; R3 = H, C1-6 alkyl optionally substituted with 1-3 substituents, (CH2)0-4-(hetero)aryl, etc.; R4 = C1-10 alkyl optionally substituted with 1-3 substituents, -(CH2)0-3-cycloalkyl, -(CR7R8)0-4-(hetero)aryl, etc.; one of R5 and R6 is H and the other is -C(O)(CR9R10)1-6-X-R11, etc.; R7 and R8 are independently selected from H, alkyl, hydroxyalkyl, alk(en/yn)yl, etc.; R9 and R10 are independently selected from H or C1-10 alkyl; R11 = (hetero)aryl, optionally substituted C1-10 alkyl, or C3-8 cycloalkyl, etc.; X = O, S, SO2, etc.]. Compds. I include inhibitors of beta-secretase enzyme useful in the treatment of Alzheimer's disease and other diseases characterized by deposition of A beta-peptide in a mammal. Biol. examples include beta-secretase inhibition, assays using synthetic oligopeptide-substrates, inhibition of A beta production in human patients, etc. For instance, compound II (preparation 8) was prepared via amidation of benzoic acid derivative III by diamino(hydroxy)propane derivative IV and subsequent Boc-cleavage (no yield data). Using 19F-NMR an intramol. acyl-migration was observed when compound II was dissolved in DMSO-d6 and pH 4 buffer solution was added.

IT 527716-85-4P 527716-94-5P 527719-92-2P

597559-71-2P 674328-18-8P 674328-19-9P

674328-20-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

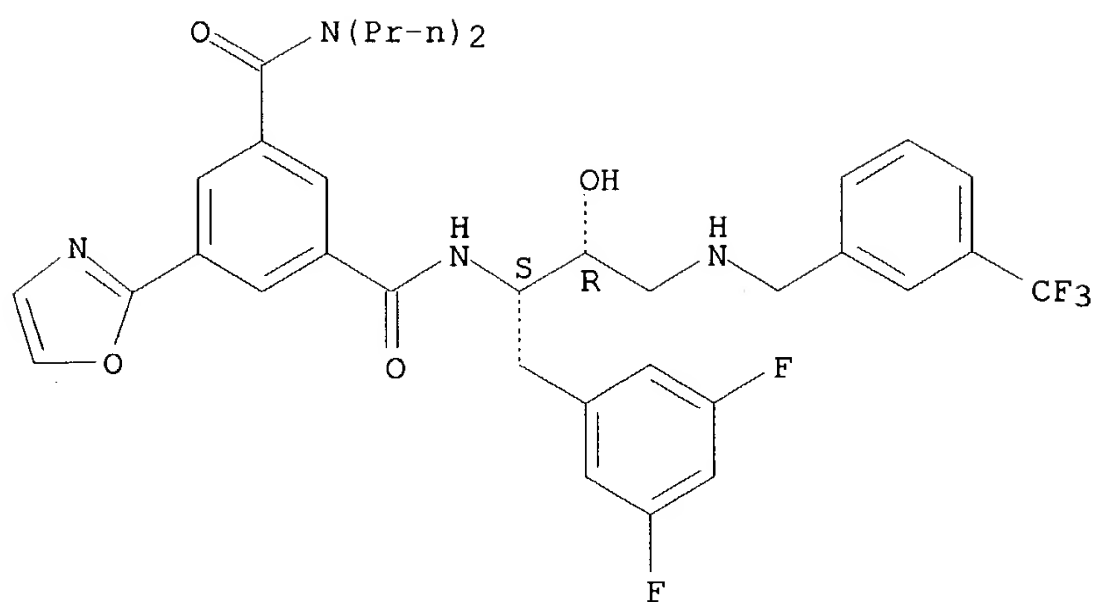
(preparation of diamino(hydroxy)propane derivs. useful as beta-secretase inhibitors)

RN 527716-85-4 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[[3-(trifluoromethyl)phenyl]methyl]amino]propyl]-5-(2-oxazolyl)-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

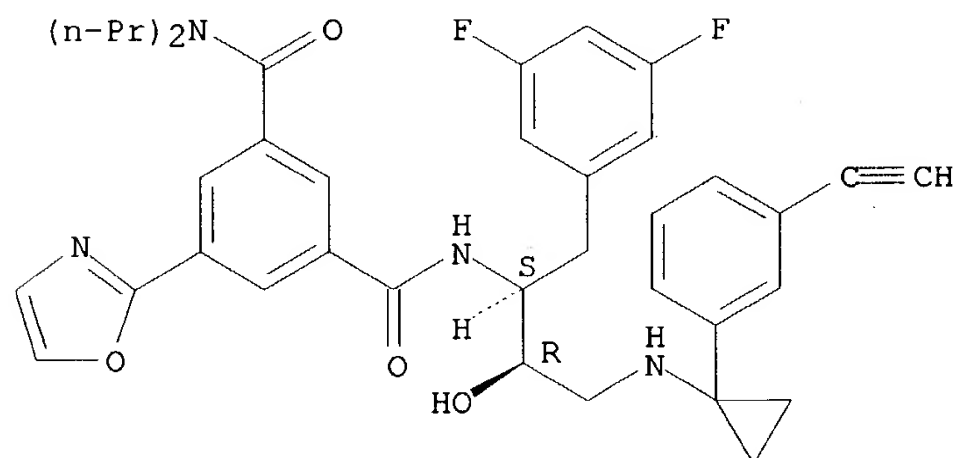
09/895,871



RN 527716-94-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[1-(3-ethynylphenyl)cyclopropyl]amino]-2-hydroxypropyl]-5-(2-oxazolyl)-N,N-dipropyl- (9CI) (CA INDEX NAME)

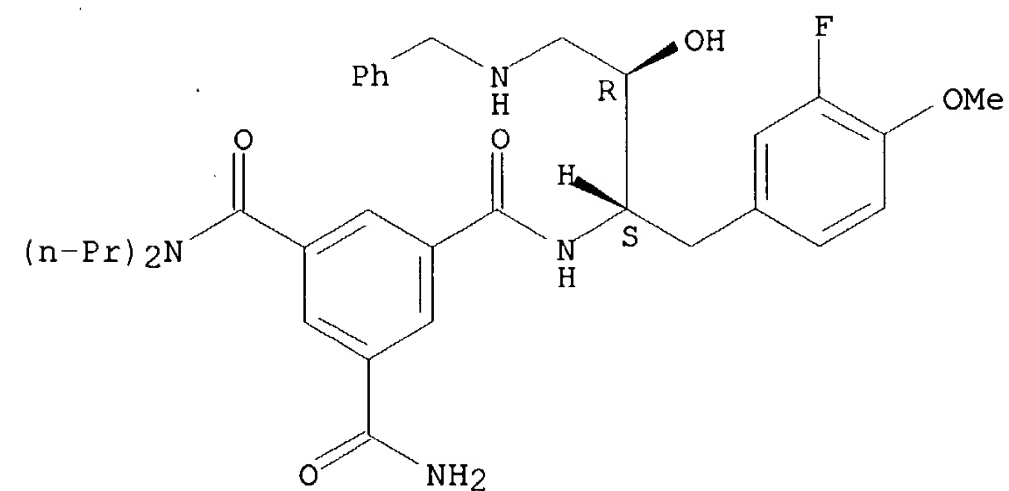
Absolute stereochemistry.



RN 527719-92-2 CAPLUS

CN 1,3,5-Benzenetricarboxamide, N'-[(1S,2R)-1-[(3-fluoro-4-methoxyphenyl)methyl]-2-hydroxy-3-[(phenylmethyl)amino]propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

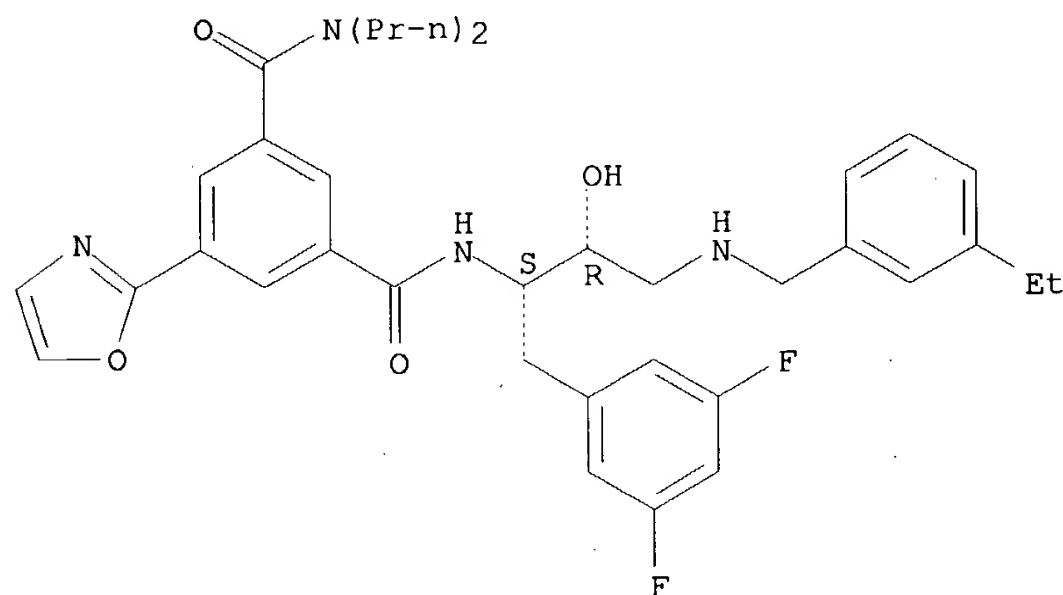


09/895,871

RN 597559-71-2 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[3-(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-(2-oxazolyl)-N,N-dipropyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

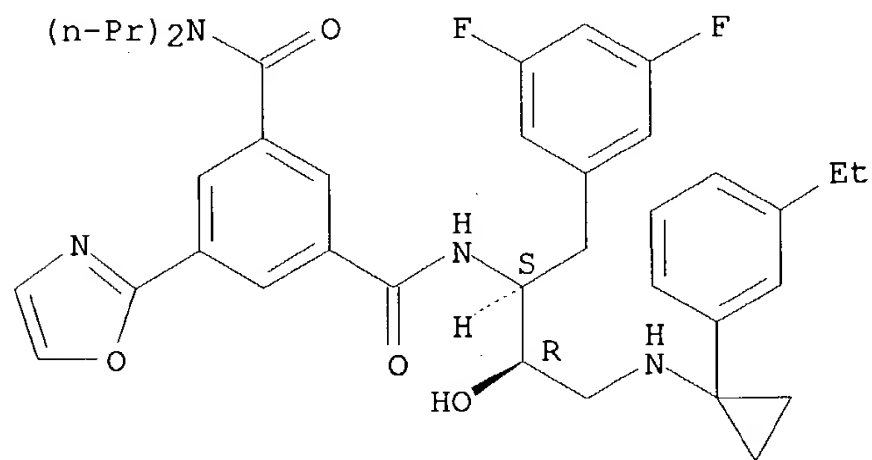


● HCl

RN 674328-18-8 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[1-(3-ethylphenyl)cyclopropyl]amino]-2-hydroxypropyl]-5-(2-oxazolyl)-N,N-dipropyl-, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



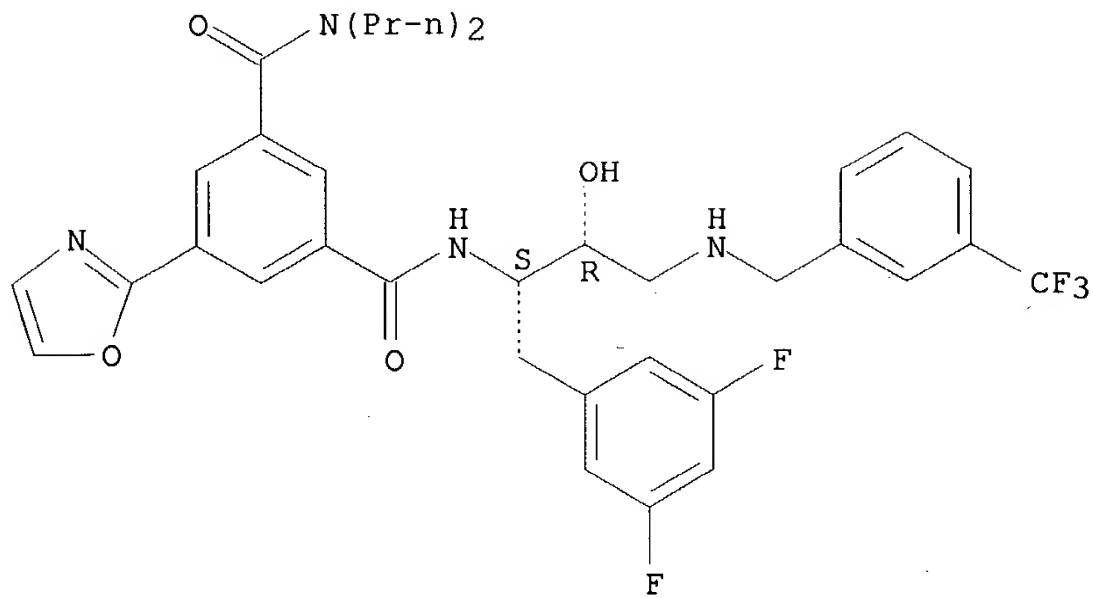
● 2 HCl

RN 674328-19-9 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[[3-(trifluoromethyl)phenyl]methyl]amino]propyl]-5-(2-oxazolyl)-N,N-dipropyl-, monohydrochloride (9CI) (CA INDEX NAME)

09/895,871

Absolute stereochemistry.

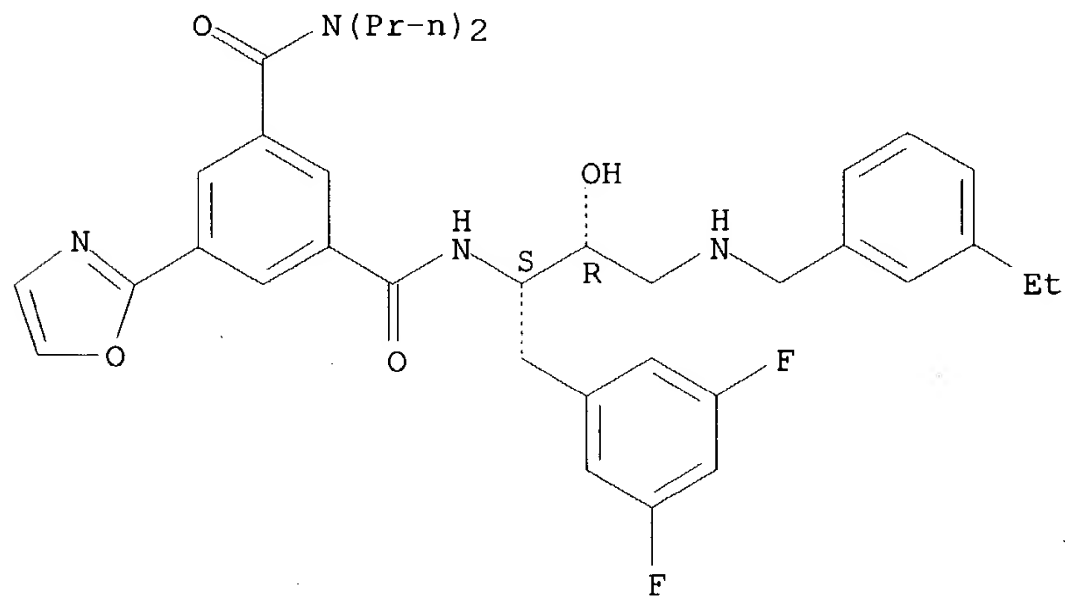


● HCl

RN 674328-20-2 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-(2-oxazolyl)-N,N-dipropyl-, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

L5 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:143093 CAPLUS

DOCUMENT NUMBER: 140:181220

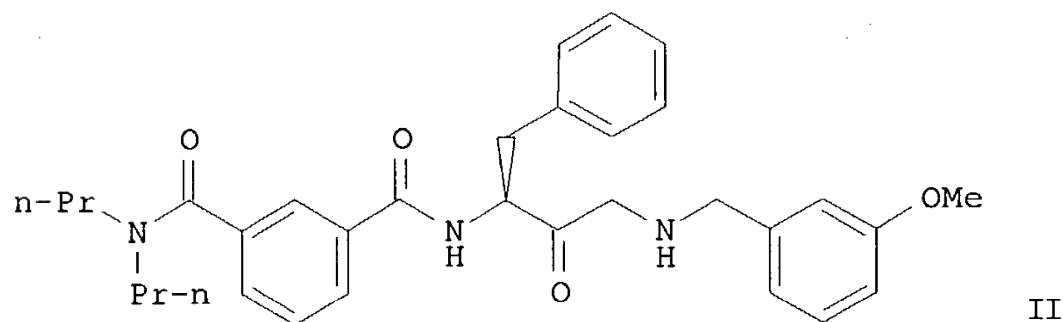
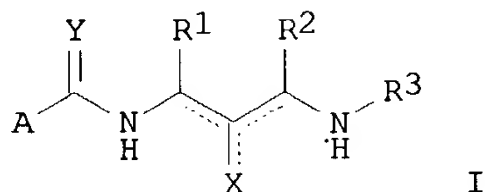
TITLE: Preparation of benzamide derivatives as β -secretase inhibitors

INVENTOR(S): Uchikawa, Osamu; Aso, Kazuyoshi; Koike, Tatsuki;

09/895,871

PATENT ASSIGNEE(S): Tarui, Naoki; Hirai, Keisuke
SOURCE: Takeda Chemical Industries, Ltd., Japan
PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014843	A1	20040219	WO 2003-JP10045	20030807
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2004091483	A2	20040325	JP 2003-288504	20030807
PRIORITY APPLN. INFO.:			JP 2002-233231	A 20020809
OTHER SOURCE(S):			MARPAT 140:181220	
GI				



AB The title compds. I [wherein A = (un)substituted aryl; R1 = (un)substituted aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkyl, cycloalkyl, or cycloalkylalkyl; R2 = H, (un)substituted aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkyl, or cycloalkyl; R3 = (un)substituted arylalkyl, heteroarylalkyl, or alkyl; X = O, S, or (un)substituted NH; Y = O or S; with exclusions] or prodrugs or salts thereof are prepared as β -secretase inhibitors. For example, the compound II•HCl was prepared in a multi-step synthesis. II•HCl showed inhibitory activity with IC₅₀ of 0.099 μ M against human β -secretase. I are useful for the treatment of neurodegenerative disease, neuropathy, memory disorder, psychiatric disorder, etc. (no data). Formulations containing I as an active ingredient were also described.

IT **388062-23-5P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

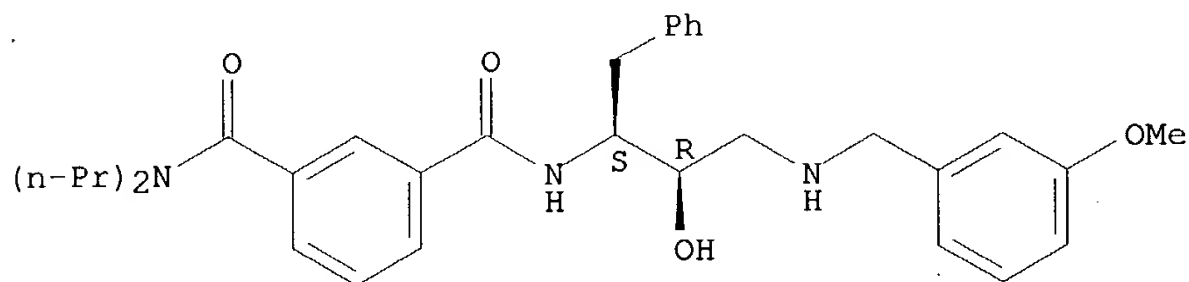
09/895,871

(intermediate; preparation of benzamide derivs. as β -secretase inhibitors)

RN 388062-23-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:133028 CAPLUS

DOCUMENT NUMBER: 140:321703

TITLE: Countering Cooperative Effects in Protease Inhibitors Using Constrained β -Strand-Mimicking Templates in Focused Combinatorial Libraries

AUTHOR(S): Reid, Robert C.; Pattenden, Leonard K.; Tyndall, Joel D. A.; Martin, Jennifer L.; Walsh, Terry; Fairlie, David P.

CORPORATE SOURCE: Centre for Drug Design and Development, Institute for Molecular Bioscience, University of Queensland, Brisbane, QLD 4072, Australia

SOURCE: Journal of Medicinal Chemistry (2004), 47(7), 1641-1651

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In this work, the authors used templates consisting of constrained cyclic tripeptides, formed through side chain to main chain linkages, as structural mimics of the protease-bound extended β -strand conformation of three adjoining amino acid residues at the N- or C-terminal sides of the scissile bond of substrates. The macrocyclic templates were derivatized to a range of 30 structurally diverse mols. composed of nonpeptidic appendages incorporating a hydroxyethylamine transition-state isostere. Most macrocycles in this library were potent inhibitors of HIV-1 protease. Comparison of crystal structures of protease-inhibitor complexes established that the macrocycles fix their surrounding enzyme environment, thereby permitting independent variation of acyclic inhibitor components with only local disturbances to the protease. In this way, the location in the protease of various acyclic fragments on either side of the macrocyclic template can be accurately predicted. This type of templating strategy minimizes the problem of induced fit, reducing unpredictable cooperative effects in one inhibitor region caused by changes to adjacent enzyme-inhibitor interactions. This idea might be exploited in template-based approaches to inhibitors of other proteases, where a β -strand mimetic is required for recognition, and also for other protein-binding ligands where different

09/895,871

templates may be more appropriate.

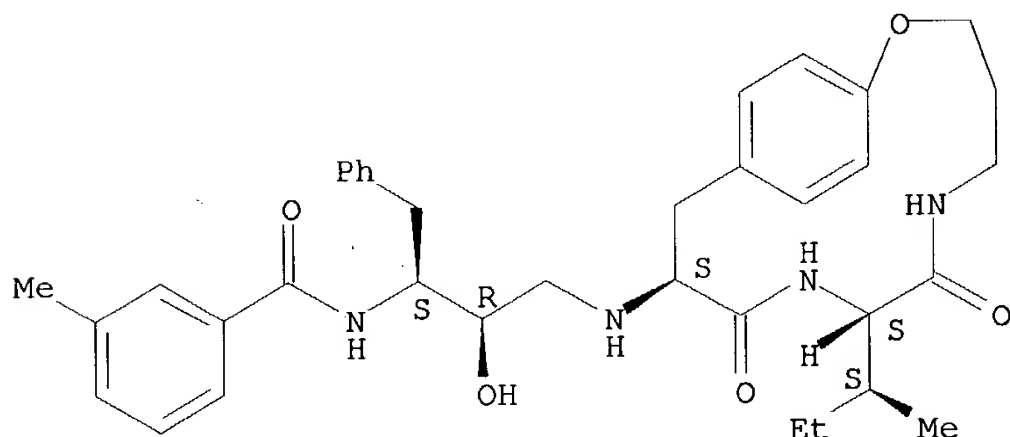
IT **679402-42-7P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of a library of HIV-1 protease inhibitors composed of β -strand-mimicking peptidyl macrocycles)

RN 679402-42-7 CAPLUS

CN Benzamide, N-[(1S,2R)-2-hydroxy-3-[[(8S,11S)-8-[(1S)-1-methylpropyl]-7,10-dioxo-2-oxa-6,9-diazabicyclo[11.2.2]heptadeca-13,15,16-trien-11-yl]amino]-1-(phenylmethyl)propyl]-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:2867 CAPLUS

DOCUMENT NUMBER: 140:59634

TITLE: Process for preparing 5-(1,3-oxazol-2-yl)benzoic acid derivatives

INVENTOR(S): Reeder, Michael R.; Imbordino, Rick J.

PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA

SOURCE: PCT Int. Appl., 55 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000821	A1	20031231	WO 2003-US19585	20030620
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004063965	A1	20040401	US 2003-600100	20030620
PRIORITY APPLN. INFO.:			US 2002-390285P	P 20020620
			US 2003-450478P	P 20030227

09/895,871

OTHER SOURCE(S): CASREACT 140:59634; MARPAT 140:59634

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed are compds. of formula (I) [R1 = C1-6 alkoxy, OH; R2, R3 = H, Ph, C1-4 alkyl; or R2 and R3 and the carbons to which they are attached form a benzo ring, which is optionally substituted with C1-4 alkyl, C1-4 alkoxy, or dialkylamino; R6 = C1-6 alkoxy or NR4R5; R4, R5 = C1-6 alkyl] and a process to prepare the compound I, by coupling a zinc chloride/optionally substituted oxazole adduct (II) (R2, R3 = same as above) and an compound of formula (III) (X = Br, iodo, OSO2CF3, OSO2Me) in the presence of a transition metal catalyst. The compds. I are used to prepare compds. of formula (IV) [R2, R3, R6 = same as above; R10 = R10 = -(CH2)1-2-S(O)0-2-(C1-6 alkyl), or each (un)substituted C1-10 alkyl, C2-6 alkenyl, or C2-6 alkynyl, aryl, heteroaryl, heterocyclyl, C1-6-alkylaryl, C1-6 alkylheteroaryl, or C1-6 alkylheterocyclyl, where the ring portions of each are optionally substituted; R20, R30 = H, each (un)substituted C1-6 alkyl, CONH2, or SO2NH2, (CH2)0-4-aryl, (CH2)0-4-heteroaryl, C2-6 alkenyl, C2-6 alkynyl, CO2H, CO2-(C1-4 alkyl); or R20, R30 and the carbon to which they are attached form a C3-7 carbocycle, wherein one carbon atom is optionally replaced by a group selected from O, S, SO2, or (un)substituted NH; Rc = H, (CR245R250)0-4-aryl, (CR245R250)0-4-heteroaryl, (CR245R250)0-4-heterocyclyl, (CR245R250)0-4-arylheteroaryl, (CR245R250)0-4-arylheterocyclyl, (CR245R250)0-4-arylaryl, (CR245R250)0-4-heteroarylaryl, (CR245R250)0-4-heteroarylheterocyclyl, (CR245R250)0-4-heteroarylheteroaryl, etc.; R245, R250 = H, C1-4 alkyl, C1-4 alkylaryl, C1-4 alkylheteroaryl, C1-4 hydroxyalkyl, C1-4 alkoxy, C1-4 haloalkoxy, (CH2)0-4-C3-7 cycloalkyl, Ph, etc.; or R245 and R250 are taken together with the carbon to which they are attached to form a C3-7 carbocycle, where one carbon atom is optionally replaced by a heteroatom selected from O, S, SO2, and (un)substituted NH] in the treatment of Alzheimer's disease and related conditions. Thus, BuLi (1.4 equiv) was added dropwise over 30 min to a stirred, cooled (-78°) mixture of 1,3-oxazole (1.3 equiv) in THF, while maintaining the mixture at a temperature bellow about -55°, stirred for 30 min, treated with solid ZnCl2 (3 equiv) in 3-10 portions over about 10-15 min, allowed to warm to 20-25°, and stirred for an addnl. 10 min to give a solution of 2-oxazolylzinc chloride. The latter zinc chloride adduct was added over a period of 2 h to a mixture of Me 3-bromo-5-[(dipropylamino)carbonyl]benzoate (V) and tetrakis(triphenylphosphine) palladium (5 mol%) in THF at 50°, and stirred at 50° until no V was observed by HPLC (usually about 1 h) to give, after workup and silica gel chromatog., Me 3-[(dipropylamino)carbonyl]-5-(1,3-oxazol-2-yl)benzoate (VI). VI was saponified by NaOH in aqueous MeOH and acidified with concentrated HCl to give 3-[(dipropylamino)carbonyl]-5-(1,3-oxazol-2-yl)benzoic acid which was treated with CDI in THF at room temperature for 1 h, added slowly over to a cooled (-35°) mixture of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol in THF, warmed to 0°, and stirred until the completion of the reaction was observed by HPLC to give, after workup and silica gel chromatog., N1-[(1S,2R)-1-(3,5-difluorobenzyl)-3-[[1-(3-ethynylphenyl)cyclopropyl]amino]-2-hydroxypropyl]-5-(1,3-oxazol-2-yl)-N3,N3-dipropylisophthalamide (VII).

IT 527716-71-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

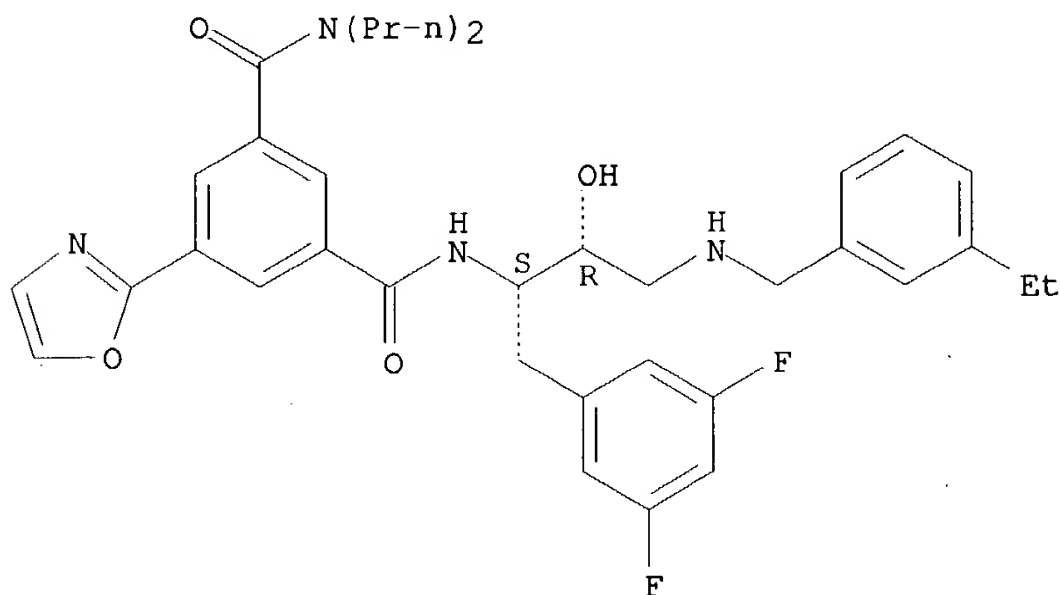
09/895,871

(process for preparing oxazolybenzoic acid derivs. as intermediates for anti-Alzheimer's agent)

RN 527716-71-8 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-(2-oxazolyl)-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:696859 CAPLUS

DOCUMENT NUMBER: 139:230480

TITLE: Preparation of substituted amines prodrugs useful in treating Alzheimer's disease

INVENTOR(S): Varghese, John; Jagodzinska, Barbara; Maillard, Michel; Beck, James P.; Tenbrink, Ruth E.; Getman, Daniel

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn

SOURCE: PCT Int. Appl., 483 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072535	A2	20030904	WO 2003-US7287	20030227
WO 2003072535	C1	20040930		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.:

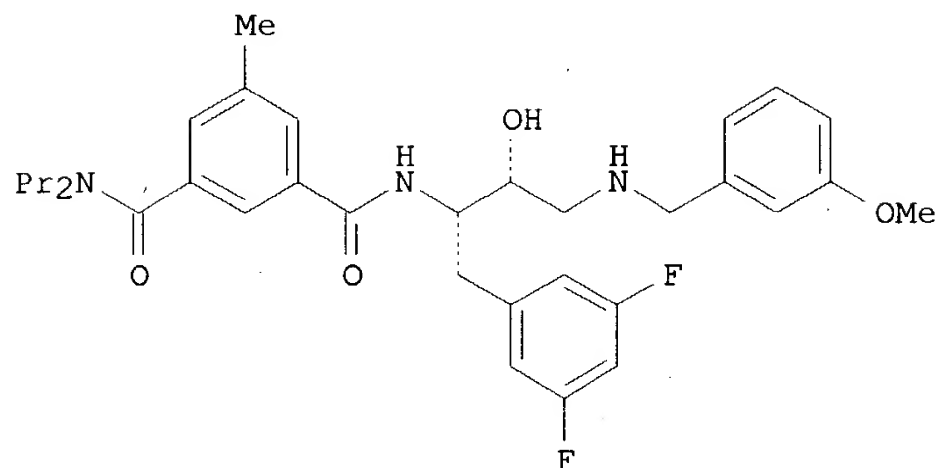
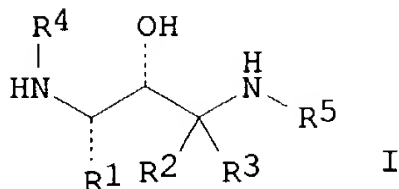
US 2002-359953P

P 20020227

OTHER SOURCE(S):

MARPAT 139:230480

GI



AB Amines [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, (un)substituted alkyl, alkenyl, etc.; R3 = H, (un)substituted alkyl, alkenyl, etc.; R4 = XR; X = CO, SO₂, a bond, etc.; R = Ph, naphthyl, indanyl, etc.; R5 = (un)substituted alkyl, (CH₂)₀₋₃cycloalkyl, etc.; e.g. N1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-methyl-N3,N3-dipropylisophthalamide], useful in treating Alzheimer's disease and other similar diseases, were prepared. Although the methods of preparation are not claimed, hundreds of example prepns. are included. Thus, reacting (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol trifluoroacetate with 5-methyl-N,N-dipropylisophthalamide in the presence of Et₃N, 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in DMF afforded (1S,2R)-II (N1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-methyl-N3,N3-dipropylisophthalamide). The compds. I exhibit an IC₅₀ of < 50 μM against β-secretase.

IT **388066-36-2P**, N-[(1R,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-bromo-5-methylbenzamide **388071-98-5P**, N-[(1S,2R)-1-[4-(Benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-N'-[4-(benzyloxy)butyl]-5-methyl-N'-propylisophthalamide

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

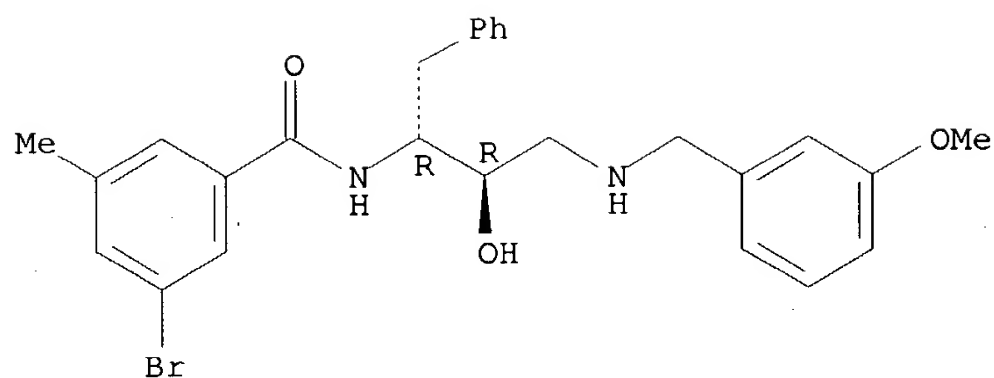
(drug candidate; preparation of substituted amine prodrugs useful in treating Alzheimer's disease)

RN 388066-36-2 CAPLUS

CN Benzamide, 3-bromo-N-[(1R,2R)-2-hydroxy-3-[[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

09/895,871

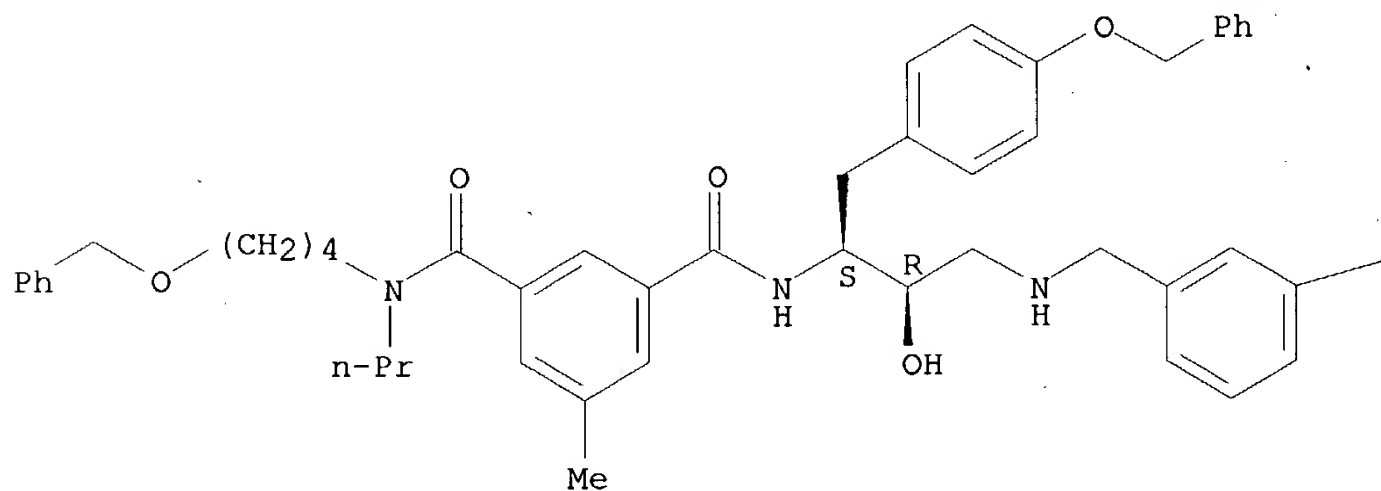


RN 388071-98-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]-1-[[4-(phenylmethoxy)phenyl)methyl]propyl]-5-methyl-N-[4-(phenylmethoxy)butyl]-N-propyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

—OMe

IT 388062-16-6P, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide
388062-17-7P, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[[2-furyl)methyl]amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide
388062-19-9P, N-[(1S,2R)-1-Benzyl-3-(benzylamino)-2-hydroxypropyl]-N',N'-dipropylisophthalamide 388062-21-3P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(4-toluidino)propyl]-N',N'-dipropylisophthalamide
388062-22-4P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-(4-methoxyphenyl)ethyl]amino]propyl]-N',N'-dipropylisophthalamide
388062-23-5P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-N',N'-dipropylisophthalamide
388062-26-8P, N-[(1S,2R)-1-Benzyl-3-[(2-chlorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide 388062-27-9P,

N-[(1S,2R)-1-Benzyl-3-[(4-chlorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-29-1P**, N-[(1S,2R)-1-Benzyl-3-(2,3-dihydro-1H-inden-1-ylamino)-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-31-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(tetrahydro-2-furanylmethyl)amino]propyl]-N',N'-dipropylisophthalamide **388062-34-8P**, N-[(1S,2R)-1-Benzyl-3-(cyclohexylamino)-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-35-9P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-pyridinyl)methyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-36-0P**, N-[(1S,2R)-3-[(2-Aminobenzyl)amino]-1-benzyl-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-37-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-pyridinyl)methyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-38-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-(1-pyrrolidinyl)ethyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-43-9P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-phenylpropyl)amino]propyl]-N',N'-dipropylisophthalamide **388062-48-4P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(4-phenylbutyl)amino]propyl]-N',N'-dipropylisophthalamide **388062-49-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-iodobenzyl)amino]propyl]-N',N'-dipropylisophthalamide **388062-51-9P**, N-[(1S,2R)-1-Benzyl-3-[(3-chlorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-52-0P**, N-[(1S,2R)-1-Benzyl-3-[[2-(4-chlorophenyl)ethyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-53-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-(2-pyridinyl)ethyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-54-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[4-(pyridinyl)methyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-56-4P**, N-[(1S,2R)-1-Benzyl-3-[(2,3-dimethylbenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-57-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-(trifluoromethoxy)benzyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-58-6P**, N-[(1S,2R)-1-Benzyl-3-[(2-chloro-6-phenoxybenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-59-7P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[4-(trifluoromethyl)benzyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-60-0P**, N-[(1S,2R)-1-Benzyl-3-[(2,3-dichlorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-61-1P**, N-[(1S,2R)-1-Benzyl-3-[(3,5-dichlorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-62-2P**, N-[(1S,2R)-1-Benzyl-3-[(3,5-difluorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-63-3P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[4-(trifluoromethoxy)benzyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-64-4P**, N-[(1S,2R)-3-[[2-[4-(Aminosulfonyl)phenyl]ethyl]amino]-1-benzyl-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-65-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(4-methoxybenzyl)amino]propyl]-N',N'-dipropylisophthalamide **388062-66-6P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(4-methylbenzyl)amino]propyl]-N',N'-dipropylisophthalamide **388062-67-7P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3,4,5-trimethoxybenzyl)amino]propyl]-N',N'-dipropylisophthalamide **388062-68-8P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[3-(trifluoromethoxy)benzyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-69-9P**, N-[(1S,2R)-1-Benzyl-3-[(3,5-dimethoxybenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-70-2P**, N-[(1S,2R)-1-Benzyl-3-[(2,4-dimethoxybenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-71-3P**, N-[(1S,2R)-1-Benzyl-3-[[[1,1'-biphenyl]-3-yl)methyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-72-4P**, N-[(1S,2R)-1-Benzyl-3-[(3,4-dichlorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-73-5P**, N-[(1S,2R)-1-Benzyl-3-[(2-fluorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-74-6P**,

N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[3-(trifluoromethyl)benzyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-75-7P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(2-methylbenzyl)amino]propyl]-N',N'-dipropylisophthalamide **388062-78-0P**, N-[(1S,2R)-1-Benzyl-3-[[3,5-bis(trifluoromethyl)benzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-79-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-(trifluoromethyl)benzyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-82-6P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(4-hydroxy-3-methoxybenzyl)amino]propyl]-N',N'-dipropylisophthalamide **388062-83-7P**, N-[(1S,2R)-1-Benzyl-3-[(3,4-dihydroxybenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-88-2P**, N-[(1S,2R)-1-Benzyl-3-[[2-(2-fluorophenyl)ethyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-89-3P**, N-[(1S,2R)-1-Benzyl-3-[[2-(3-fluorophenyl)ethyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-90-6P**, N-[(1S,2R)-1-Benzyl-3-[[2-(4-fluorophenyl)ethyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-91-7P**, N-[(1S,2R)-1-Benzyl-3-[[2-(4-bromophenyl)ethyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-92-8P**, N-[(1S)-1-Benzyl-2-hydroxy-3-[[2-(3-methoxyphenyl)ethyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-93-9P**, N-[(1S,2R)-1-Benzyl-3-[[2-(2,4-dichlorophenyl)ethyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-94-0P**, N-[(1S,2R)-1-Benzyl-3-[[2-(3-chlorophenyl)ethyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-95-1P**, N-[(1S)-1-Benzyl-3-[[2-(2,5-dimethoxyphenyl)ethyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-96-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-(4-methylphenyl)ethyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-98-4P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[3-(4-morpholinyl)propyl]amino]propyl]-N',N'-dipropylisophthalamide **388063-00-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-(4-morpholinyl)ethyl]amino]propyl]-N',N'-dipropylisophthalamide **388063-02-3P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-(2-thienyl)ethyl]amino]propyl]-N',N'-dipropylisophthalamide **388063-05-6P**, N-[(1S,2R)-1-Benzyl-3-[(2,4-dichlorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-07-8P**, N-[(1S,2R)-1-Benzyl-3-[(4-tert-butylbenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-09-0P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[[(1R,2S)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amino]propyl]-N',N'-dipropylisophthalamide **388063-10-3P**, N-[(1S,2R)-1-Benzyl-3-[(3,4-dimethylbenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-18-1P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-22-7P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[[4-(dimethylamino)benzyl]amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-26-1P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[[3-pyridinyl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-32-9P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(2-phenylethyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-38-5P**, N-[(1S,2R)-3-(Cyclohexylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-43-2P**, N-[(1S,2R)-3-[(3-Chlorobenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-44-3P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-[(2-propylpentyl)sulfonyl]benzamide **388063-45-4P**, N-[(1S,2R)-3-[[[(1,1'-Biphenyl]-3-yl)methyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-46-5P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl]-5-methyl-N',N'-

dipropylisophthalamide **388063-47-6P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-methylbenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-49-8P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(1,3-thiazol-5-yl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-50-1P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(2-thienyl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-51-2P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(5-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-52-3P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(2-pyrazinyl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-53-4P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3,5-difluorobenzyl)amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-54-5P**, N-[(1S,2R)-3-[(1,3-Benzodioxol-5-yl)methyl]amino]-1-benzyl-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-55-6P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3,5-dimethoxybenzyl)amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-56-7P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-(trifluoromethyl)benzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-57-8P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(7-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-58-9P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-(trifluoromethoxy)benzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-59-0P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-fluorobenzyl)amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-60-3P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-isopropoxybenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-61-4P**, N-[(1S,2R)-3-[(3-Bromobenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-62-5P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(5-methyl-2-furyl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-64-7P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methoxy-N',N'-dipropylisophthalamide **388063-65-8P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-66-9P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-chloro-N',N'-dipropylisophthalamide **388063-68-1P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-fluoro-N',N'-dipropylisophthalamide **388063-72-7P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-3-[(4-morpholinyl)carbonyl]benzamide **388063-73-8P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methylbenzyl)amino]propyl]-N',N'-dipropylisophthalamide **388063-80-7P**, 3-Benzoyl-N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]benzamide **388063-81-8P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl][1,1'-biphenyl]-3-carboxamide **388063-82-9P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-N'-(2-methoxyethyl)-N'-propylisophthalamide **388063-83-0P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-ethoxybenzamide **388063-84-1P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-2-naphthamide **388063-85-2P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(1R)-1,2,3,4-tetrahydronaphthalen-1-yl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-86-3P**, N-[(1R)-3-[[3,5-Bis(trifluoromethyl)benzyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-87-4P**,

N-[(1S,2R)-1-Benzyl-3-[[2-fluoro-5-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-88-5P**,
 N-[(1S,2R)-1-Benzyl-3-[(2,3-difluorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-89-6P**, N-[(1S,2R)-1-Benzyl-3-[[3-fluoro-4-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-90-9P**, N-[(1S,2R)-1-Benzyl-3-[(2,5-difluorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-91-0P**, N-[(1S,2R)-1-Benzyl-3-[[3-fluoro-5-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-92-1P**, N-[(1S,2R)-1-Benzyl-3-[(3,4-difluorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-93-2P**, N-[(1S,2R)-1-Benzyl-3-[[4-fluoro-3-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-94-3P**, N-[(1S,2R)-1-Benzyl-3-[[2-chloro-5-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-95-4P**, N-[(1S,2R)-1-Benzyl-3-[[4-chloro-3-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-96-5P**, N-[(1S,2R)-1-Benzyl-3-(2,3-dihydro-1H-inden-2-ylamino)-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-97-6P**, N-[(1S)-1-Benzyl-2-hydroxy-3-[(3-nitrobenzyl)amino]propyl]-N',N'-dipropylisophthalamide **388063-98-7P**, N-[(1S,2R)-1-Benzyl-3-[[3-(difluoromethoxy)benzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-99-8P**, N-[(1S,2R)-1-Benzyl-3-[(3-ethoxybenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388064-00-4P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[5-methyl-2-pyrazinyl)methyl]amino]propyl]-N',N'-dipropylisophthalamide **388064-01-5P**, N-[(1S,2R)-1-Benzyl-3-[(3-bromo-4-fluorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388064-02-6P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3,5-dimethylbenzyl)amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-03-7P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethoxybenzyl)amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-05-9P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-isobutoxybenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-06-0P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[[4-methyl-1,3-thiazol-2-yl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-07-1P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-N'-methyl-N'-propylisophthalamide **388064-13-9P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(1R)-7-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-14-0P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(1S)-7-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-15-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-(dimethylamino)benzamide **388064-16-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-2-methyl-1H-benzimidazole-5-carboxamide **388064-17-3P**, 3-(Aminosulfonyl)-N-[(1S)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-4-chlorobenzamide **388064-18-4P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-cyanobenzamide **388064-19-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-4-chloro-3-nitrobenzamide **388064-20-8P**, Methyl 3-[[[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]amino]carbonyl]-5-nitrobenzoate **388064-21-9P**, tert-Butyl [3-[[[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]amino]carbonyl]phenyl]carbamate **388064-22-0P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-9,10-dioxo-9,10-dihydro-2-

anthracenecarboxamide **388064-23-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-1H-1,2,3-benzotriazole-6-carboxamide **388064-24-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-4-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)benzamide **388064-25-3P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-1H-indole-5-carboxamide **388064-26-4P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-fluoro-5-(trifluoromethyl)benzamide **388064-27-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-(trifluoromethyl)benzamide **388064-28-6P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-4-(butylamino)benzamide **388064-29-7P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-(trifluoromethoxy)benzamide **388064-30-0P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3,5-dimethoxybenzamide **388064-31-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3,5-dimethylbenzamide **388064-32-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3,5-difluorobenzamide **388064-33-3P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3,5-dichlorobenzamide **388064-34-4P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-4-(benzyloxy)benzamide **388064-35-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-1,3-benzodioxole-5-carboxamide **388064-36-6P**, 3-(Acetylamino)-N-[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]benzamide **388064-37-7P**, 4-(Acetylamino)-N-[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]benzamide **388064-38-8P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[[3,5-dimethyl-4-isoxazolyl)methyl]amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-39-9P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-phenylpropyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-40-2P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[[3-furyl)methyl]amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-42-4P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-propoxybenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-43-5P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[[2-pyridinyl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-44-6P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-hydroxy-N',N'-dipropylisophthalamide **388064-46-8P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(1S)-1,2,3,4-tetrahydronaphthalen-1-yl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-47-9P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(2,5-dimethylbenzyl)amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-48-0P**, N-[(1S,2R)-3-[[2-Chloro-5-(trifluoromethyl)benzyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-49-1P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(2-hydroxy-5-methylbenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-50-4P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[[2,3-dihydro-1H-inden-1-yl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-51-5P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-((1R)-2,3-dihydro-1H-inden-1-ylamino)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-53-7P**, N-[(1S,2R)-3-[[1-Benzofuran-2-yl)methyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-55-9P**, N-[(1S,2R)-1-(4-Fluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-56-0P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-[butyl(butyryl)amino]-5-methylbenzamide **388064-57-1P**, N-[1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-4-methyl-N',N'-

dipropylisophthalamide **388064-58-2P**, N'-[1-Benzyl-2-hydroxy-3-
 [(3-methoxybenzyl)amino]propyl]-4-methyl-N,N-dipropylisophthalamide
388064-59-3P, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-
 methoxybenzyl)amino]propyl]-4-methyl-N',N'-dipropylisophthalamide
388064-60-6P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-
 methoxybenzyl)amino]propyl]-1-butyl-1H-indole-6-carboxamide
388064-61-7P, N-[(1S,2R)-3-Anilino-1-(3,5-difluorobenzyl)-2-
 hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-62-8P**
 , 5-Bromo-N-[(1S,2R)-3-[(3-bromobenzyl)amino]-1-(3,5-difluorobenzyl)-2-
 hydroxypropyl]-N',N'-dipropylisophthalamide **388064-65-1P**,
 N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-
 hydroxybenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide
388064-66-2P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-
 methoxybenzyl)amino]propyl]-5-cyano-N',N'-dipropylisophthalamide
 hydrochloride **388064-67-3P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-
 methoxybenzyl)amino]propyl]-N',N'-dipropyl-1,3,5-benzenetricarboxamide
388064-70-8P, 5-(Aminosulfonyl)-N-[(1S,2R)-1-benzyl-2-hydroxy-3-
 [(3-methoxybenzyl)amino]propyl]-N',N'-dipropylisophthalamide
388064-71-9P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-
 methoxybenzyl)amino]propyl]-N',N'-dipropyl-5-[(1-
 pyrrolidinyl)sulfonyl]isophthalamide **388064-72-0P**,
 N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-
 [(methylamino)sulfonyl]-N',N'-dipropylisophthalamide **388064-73-1P**
 , N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-
 [(dimethylamino)sulfonyl]-N',N'-dipropylisophthalamide
388064-96-8P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-
 methoxybenzyl)amino]propyl]-5-ethyl-N',N'-dipropylisophthalamide
388064-97-9P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-
 methoxybenzyl)amino]propyl]-5-isobutyl-N',N'-dipropylisophthalamide
388064-98-0P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-
 methoxybenzyl)amino]propyl]-5-tert-butyl-N',N'-dipropylisophthalamide
388064-99-1P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-
 methoxybenzyl)amino]propyl]-5-cyano-N'-propylisophthalamide
388065-00-7P, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-
 methoxybenzyl)amino]propyl]-N',N'-dipropyl-1,3,5-benzenetricarboxamide
388065-01-8P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-
 methoxybenzyl)amino]propyl]-N',N'-dimethyl-N',N'-dipropyl-1,3,5-
 benzenetricarboxamide **388065-04-1P**, N-[(1S,2R)-1-Benzyl-2-
 hydroxy-3-[(3-methoxybenzyl)amino]propyl]-N'-propyl-1,3,5-
 benzenetricarboxamide **388065-05-2P**, N-[(1S,2R)-1-Benzyl-2-
 hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-[(butyryl)(propyl)amino]-5-
 methylbenzamide **388065-06-3P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-
 [(3-methoxybenzyl)amino]propyl]-1-propyl-1H-indole-6-carboxamide
388065-07-4P, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-
 methoxybenzyl)amino]propyl]-1-propyl-1H-indole-6-carboxamide
388065-08-5P, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3,4-
 dimethylbenzyl)amino]-2-hydroxypropyl]-5-methyl-N',N'-
 dipropylisophthalamide **388065-09-6P**, N-[(1S,2R)-3-[(3-
 Aminobenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-
 dipropylisophthalamide **388065-13-2P**, N-[(1S,2R)-1-(3,5-
 Difluorobenzyl)-2-hydroxy-3-[(1R,2S)-2-hydroxy-2,3-dihydro-1H-inden-1-
 yl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide
388065-14-3P, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-
 iodobenzyl)amino]propyl]-3-methylbenzamide **388065-15-4P**,
 N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(1H-isoindol-3-
 yl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide
388065-16-5P, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-
 [(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)amino]propyl]-5-methyl-N',N'-
 dipropylisophthalamide **388065-19-8P**,
 N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-

hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388065-20-1P**,
 N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[[3-(dimethylamino)benzyl]amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388065-21-2P**,
 N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[[4,5-dimethyl-2-furyl)methyl]amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388065-22-3P**,
 N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(1-phenylcyclopentyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-23-4P**,
 N-[(1S,2R)-3-(Cyclopropylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388065-24-5P**,
 N-[(1S,2R)-3-[(Cyclopropylmethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388065-27-8P**,
 N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(tetrahydro-3-furanyl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-29-0P**,
 N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(2-oxo-3-azepanyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-30-3P**,
 N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-methyl-2-furyl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-31-4P**,
 N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[[[(2S)-tetrahydrofuran-2-yl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-33-6P**,
 N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-isopropenylbenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-36-9P**,
 N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl]-4-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)benzamide **388065-37-0P**,
 Methyl 4-[[[(2R,3S)-4-(3,5-difluorophenyl)-3-[[3-[(dipropylamino)carbonyl]-5-methylbenzoyl]amino]-2-hydroxybutyl]amino]methyl]benzoate **388065-39-2P**,
 N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[[5-isoxazolyl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-42-7P**,
 N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(2-methoxybenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-43-8P**,
 N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-44-9P**,
 4-(Butyrylamino)-N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl]benzamide
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

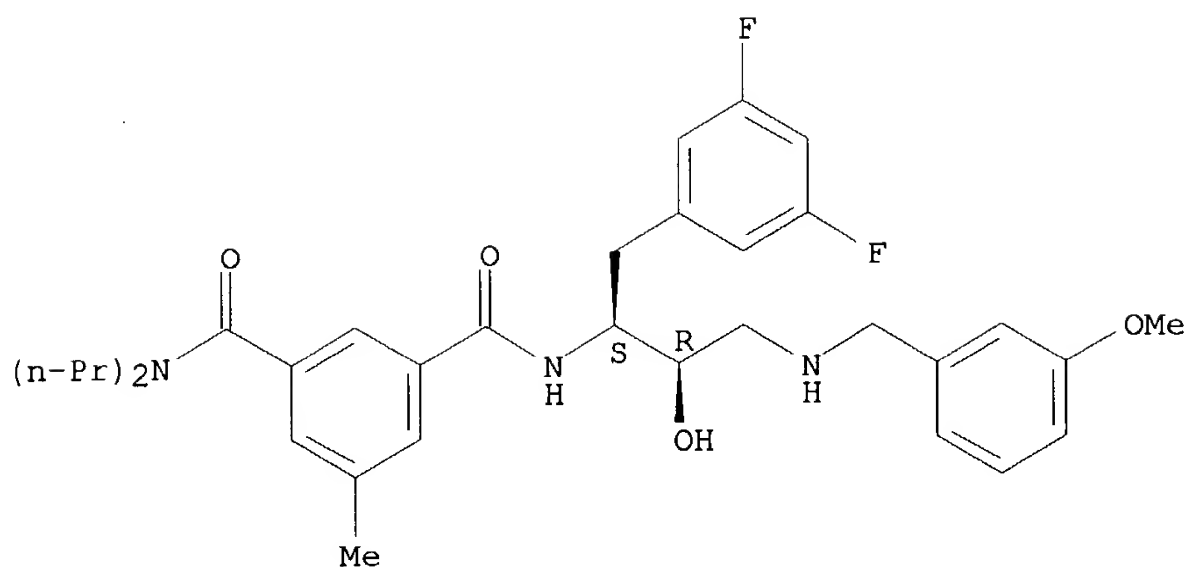
(drug candidate; preparation of substituted amine prodrugs useful in treating Alzheimer's disease)

RN 388062-16-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

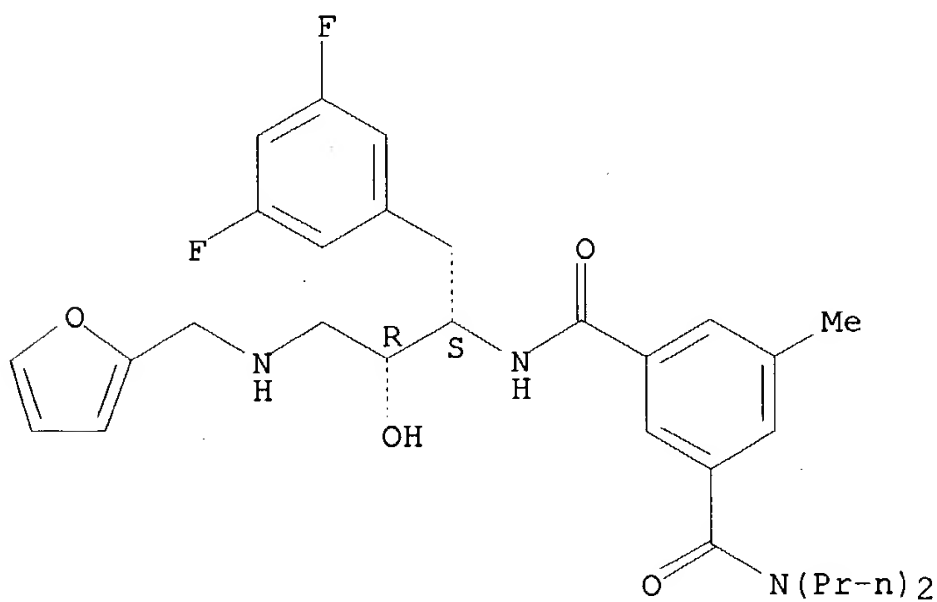
Absolute stereochemistry.

09/895,871



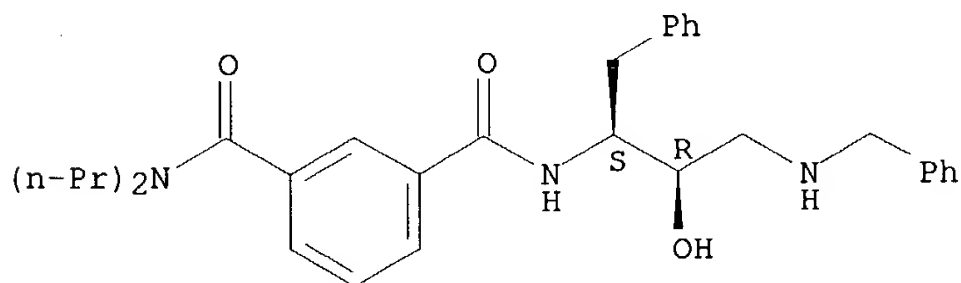
RN 388062-17-7 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[(2-furanylmethyl)amino]-2-hydroxypropyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 388062-19-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[(phenylmethyl)amino]propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

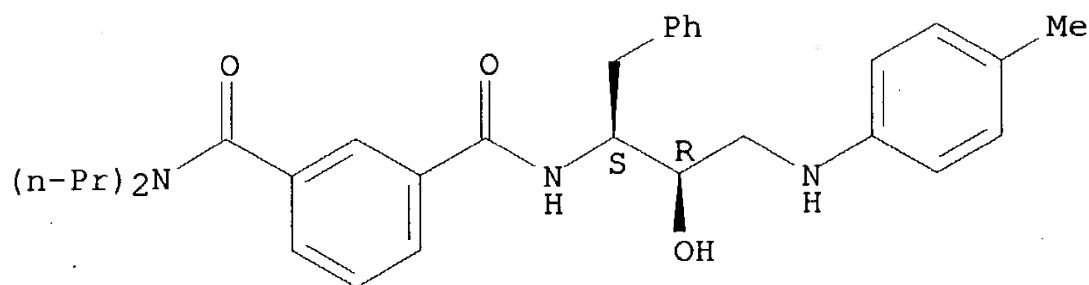


RN 388062-21-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[(4-methylphenyl)amino]-

09/895,871

1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

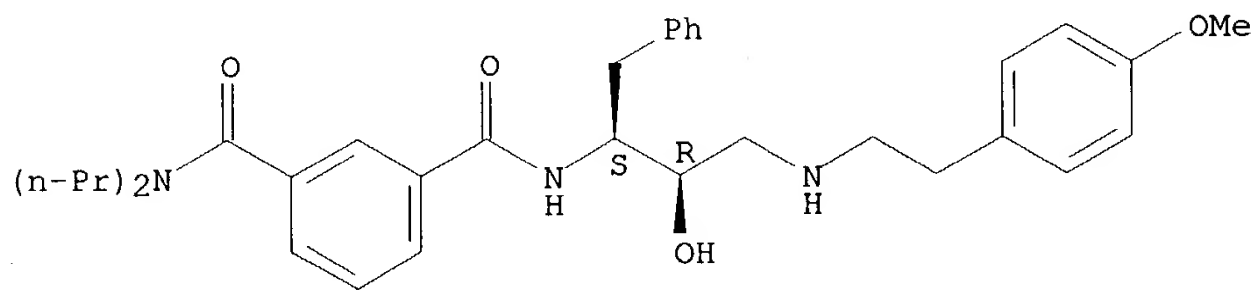
Absolute stereochemistry.



RN 388062-22-4 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[2-(4-methoxyphenyl)ethyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI)
(CA INDEX NAME)

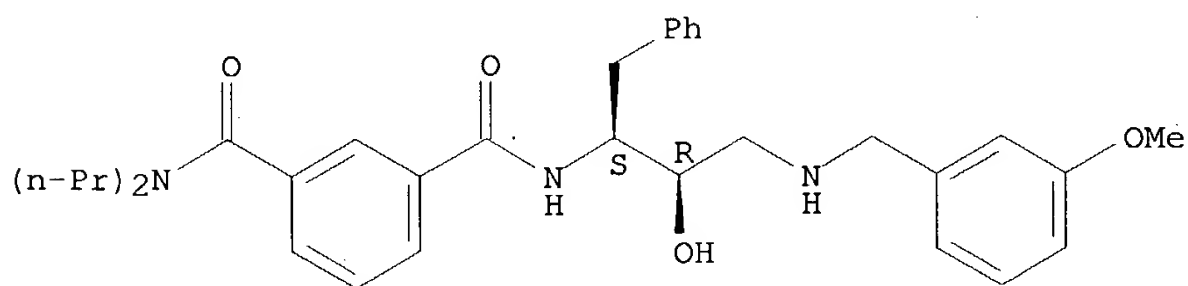
Absolute stereochemistry.



RN 388062-23-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI)
(CA INDEX NAME)

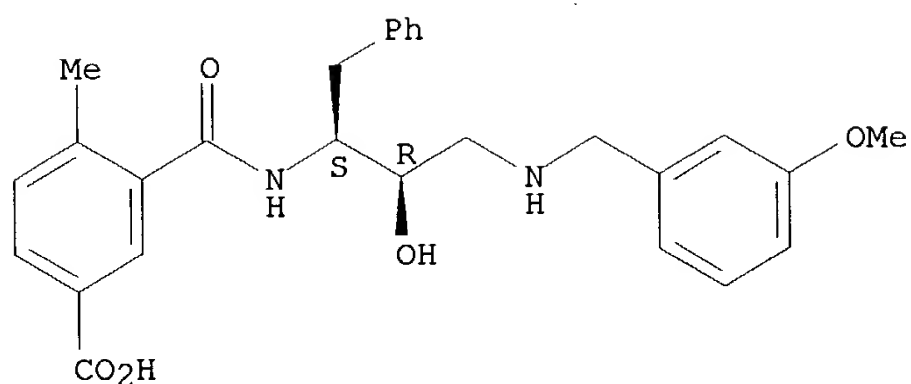
Absolute stereochemistry.



RN 388062-26-8 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-[[2-chlorophenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

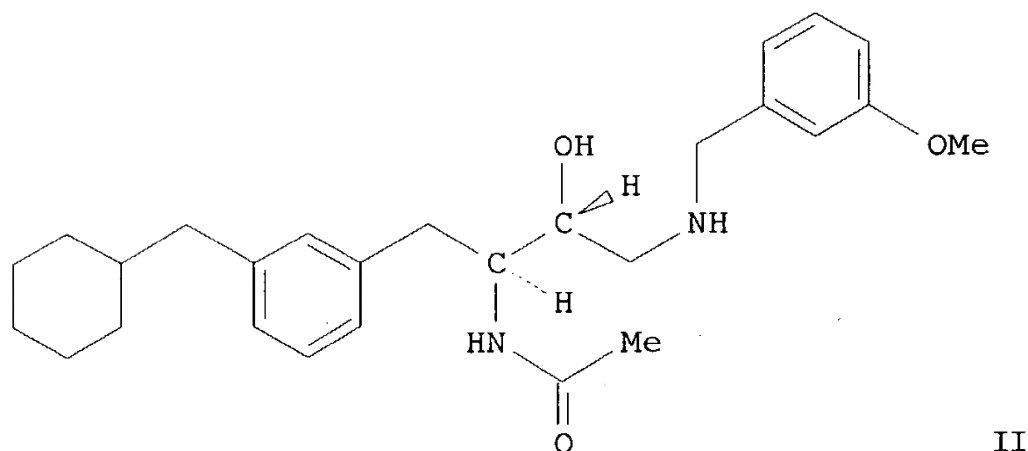
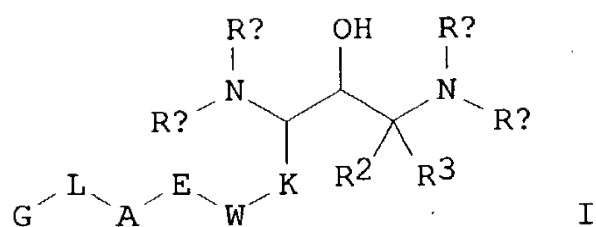
Absolute stereochemistry.



L5 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2003:472477 CAPLUS
 DOCUMENT NUMBER: 139:52753
 TITLE: Preparation of substituted hydroxyethylamines as
 β -secretase inhibitors
 INVENTOR(S): Tenbrink, Ruth; Maillard, Michel; Warpehoski, Martha
 PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn
 Company
 SOURCE: PCT Int. Appl., 306 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003050073	A1	20030619	WO 2002-US39050	20021206
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004044072	A1	20040304	US 2002-313849	20021206
EP 1453788	A1	20040908	EP 2002-795769	20021206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002014736	A	20041123	BR 2002-14736	20021206
PRIORITY APPLN. INFO.:			US 2001-338452P	P 20011206
			WO 2002-US39050	W 20021206

OTHER SOURCE(S): MARPAT 139:52753
 GI



AB Title compds. I [E = bond, alkylene; RA = H, benzyloxycarbonyl; RD = H, alkoxy carbonyl; K = (un)substituted alkyl; A = aryl, cycloalkyl, heteroaryl, etc.; W = bond, SOO-2, (un)substituted amino; L = bond, absent, etc.; G = absent, alkyl, cycloalkyl, etc.; R2-3 = H, alkyl, aryl, etc.; RN = Ph naphthyl, tetralinyl, etc.; RC = heteroaryl, etc.] are prepared as β -secretase inhibitors. For instance, N-[(1S,2R)-1-[3-(cyclohexylmethyl)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]acetamide (II) isolated as the HCl salt is prepared in several steps. The key intermediate in the synthesis is derived from the asym. hydrogenation of Me 2-[[(benzyloxy) carbonyl] amino]-3-(2-bromophenyl)acrylate (preparation given) to give the corresponding phenylalanine analog intermediate. I are useful for the treatment of Alzheimer's disease.

IT **527722-73-2P 527722-74-3P**

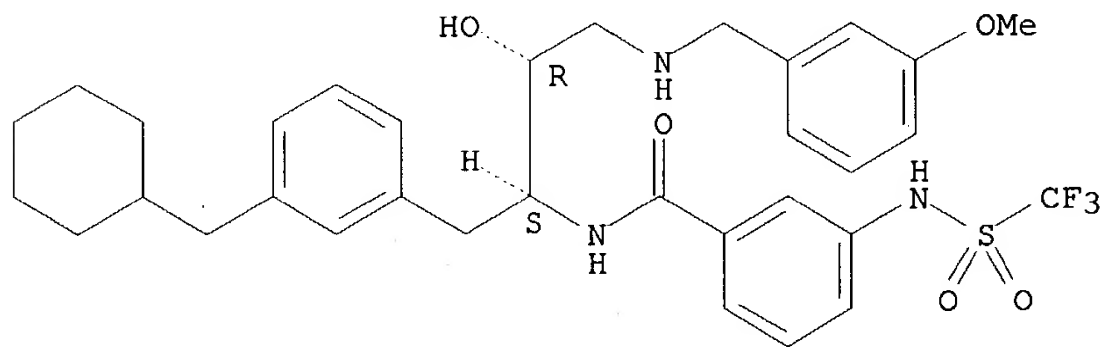
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of substituted hydroxyethylamines as β -secretase inhibitors)

RN 527722-73-2 CAPLUS

CN Benzamide, N-[(1S,2R)-1-[[3-(cyclohexylmethyl)phenyl]methyl]-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]propyl]-3-[[(trifluoromethyl)sulfonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

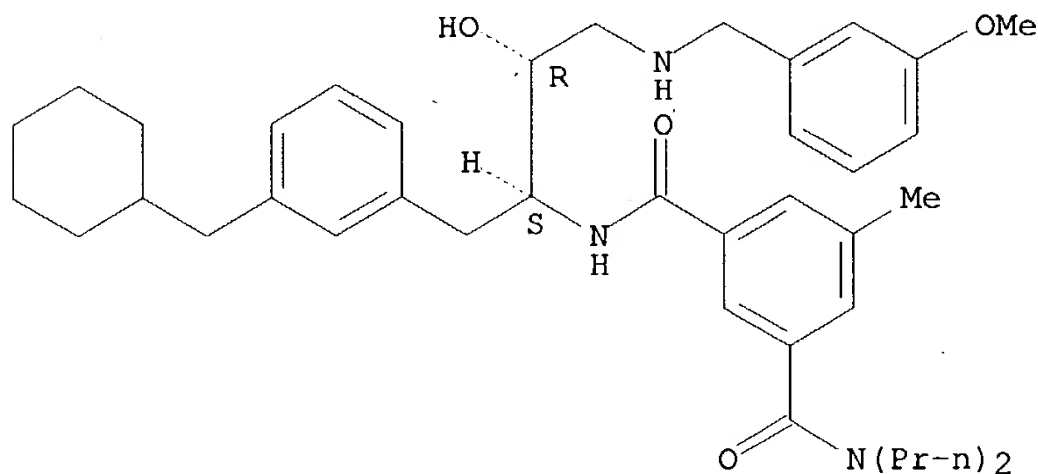


09/895,871

RN 527722-74-3 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[[3-(cyclohexylmethyl)phenyl]methyl]-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 527730-33-2P 546115-11-1P 546115-12-2P

546115-31-5P 546115-32-6P

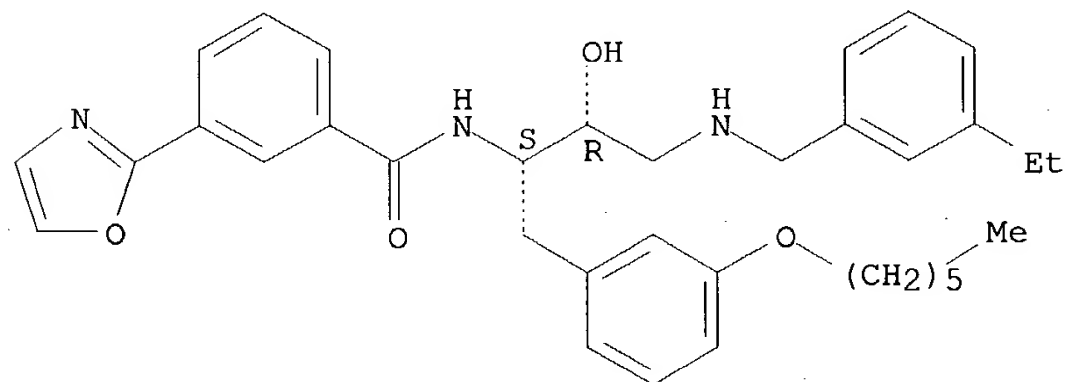
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted hydroxyethylamines as β -secretase inhibitors)

RN 527730-33-2 CAPLUS

CN Benzamide, N-[(1S,2R)-3-[[3-ethylphenyl)methyl]amino]-1-[[3-(hexyloxy)phenyl]methyl]-2-hydroxypropyl]-3-(2-oxazolyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

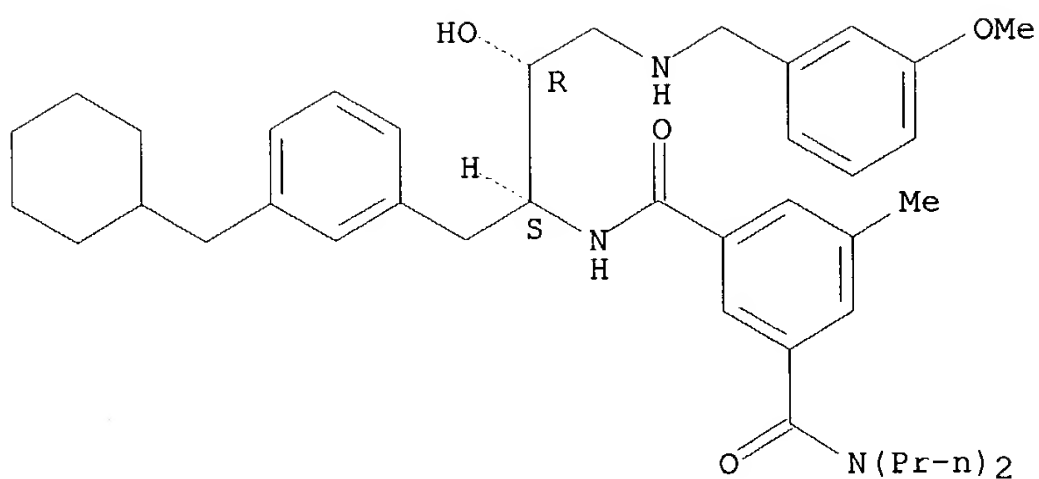


RN 546115-11-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[[3-(cyclohexylmethyl)phenyl]methyl]-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

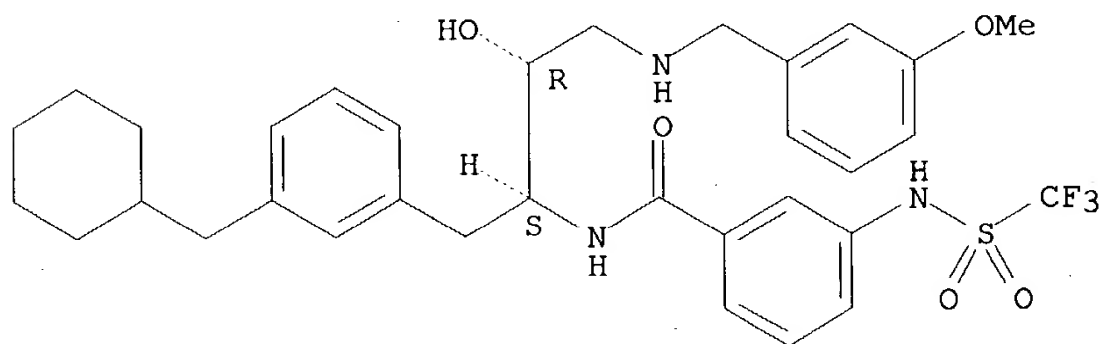
09/895,871



● HCl

RN 546115-12-2 CAPLUS
CN Benzamide, N-[(1S,2R)-1-[[3-(cyclohexylmethyl)phenyl]methyl]-2-hydroxy-3-
[[3-methoxyphenyl]methyl]amino]propyl]-3-[[trifluoromethyl]sulfonyl]amin
o]-, monohydrochloride (9CI) (CA INDEX NAME)

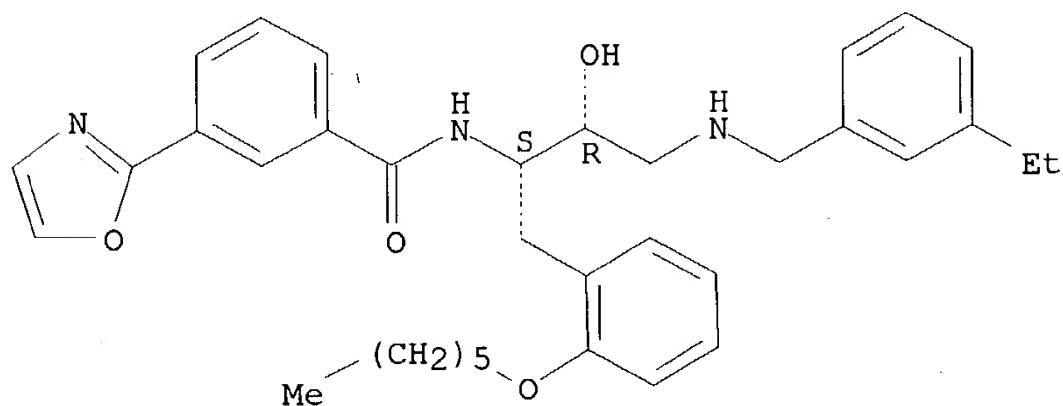
Absolute stereochemistry.



● HCl

RN 546115-31-5 CAPLUS
CN Benzamide, N-[(1S,2R)-3-[[3-ethylphenyl]methyl]amino]-1-[[2-
(hexyloxy)phenyl]methyl]-2-hydroxypropyl]-3-(2-oxazolyl)- (9CI) (CA INDEX
NAME)

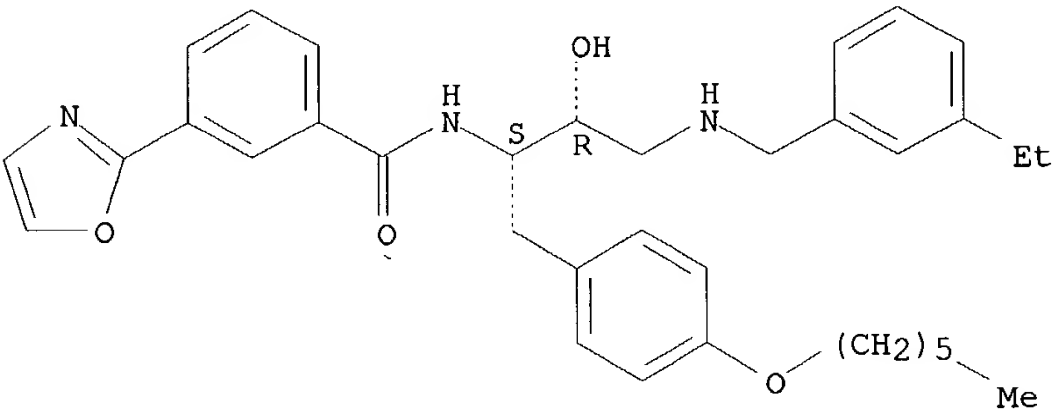
Absolute stereochemistry.



09/895,871

RN 546115-32-6 CAPLUS
CN Benzamide, N-[(1S,2R)-3-[[(3-ethylphenyl)methyl]amino]-1-[[4-(hexyloxy)phenyl]methyl]-2-hydroxypropyl]-3-(2-oxazolyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:412801 CAPLUS
DOCUMENT NUMBER: 139:245782
TITLE: Preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease
INVENTOR(S): Varghese, John; Maillard, Michel; Jagodzinska, Barbara; Beck, James P.; Gailunas, Andrea; Fang, Larry; Sealy, Jennifer; Tenbrink, Ruth; Freskos, John; Mickelson, John; Samala, Lakshman; Hom, Roy
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company
SOURCE: PCT Int. Appl., 1243 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040096	A2	20030515	WO 2002-XA36072	20021108
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2003040096	A2	20030515	WO 2002-US36072	20021108
WO 2003040096	A3	20040506		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

09/895,871

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

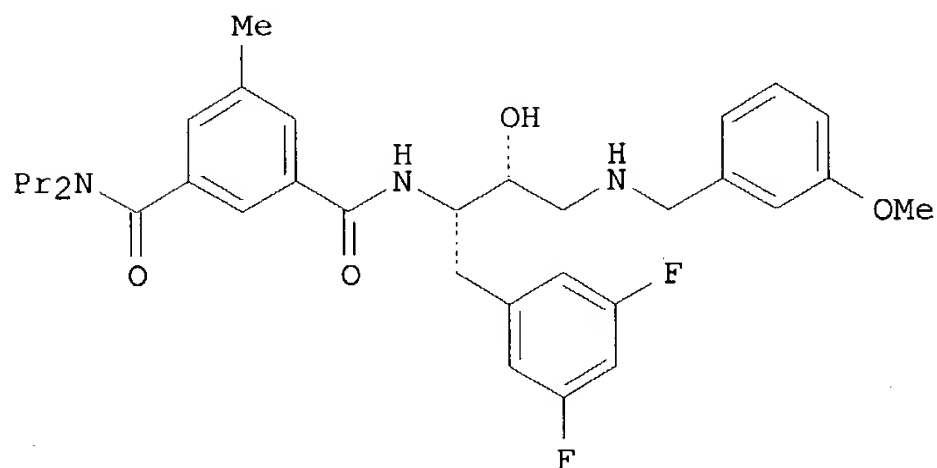
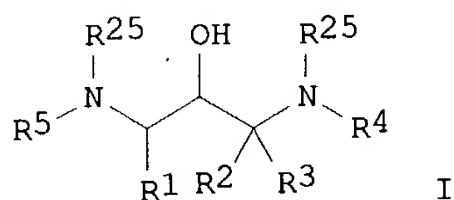
PRIORITY APPLN. INFO.:

US 2001-337122P P 20011108
US 2001-344086P P 20011228
US 2002-345635P P 20020103
WO 2002-US36072 A 20021108

OTHER SOURCE(S):

MARPAT 139:245782

GI



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, alkyl, haloalkyl, alkenyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; or R2 and R3 are taken together with the carbon to which they are attached to form a carbocycle of 3-7 carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of O, S, SO₂, (un)substituted NH; R4 = alkyl, haloalkyl, hydroxyalkyl, etc.; R5 = R6X (wherein X = CO, SO₂, (un)substituted CH₂; R6 = (un)substituted Ph, naphthyl, indanyl, etc.); R25 = H, alkyl, alkoxy, etc.] which have activity as inhibitors of β -secretase and are therefore useful in treating a variety of disorders such as Alzheimer's disease, were prepared E.g., a multi-step synthesis of (1S,2R)-II, starting from (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5-difluorophenyl)propanoic acid, was given. The compds. I showed IC₅₀ of < 20 μ M in cell free inhibition assay utilizing a synthetic APP substrate. This is a Part 2 of 1-2 series.

IT 527728-59-2P 527731-65-3P 527733-02-4P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

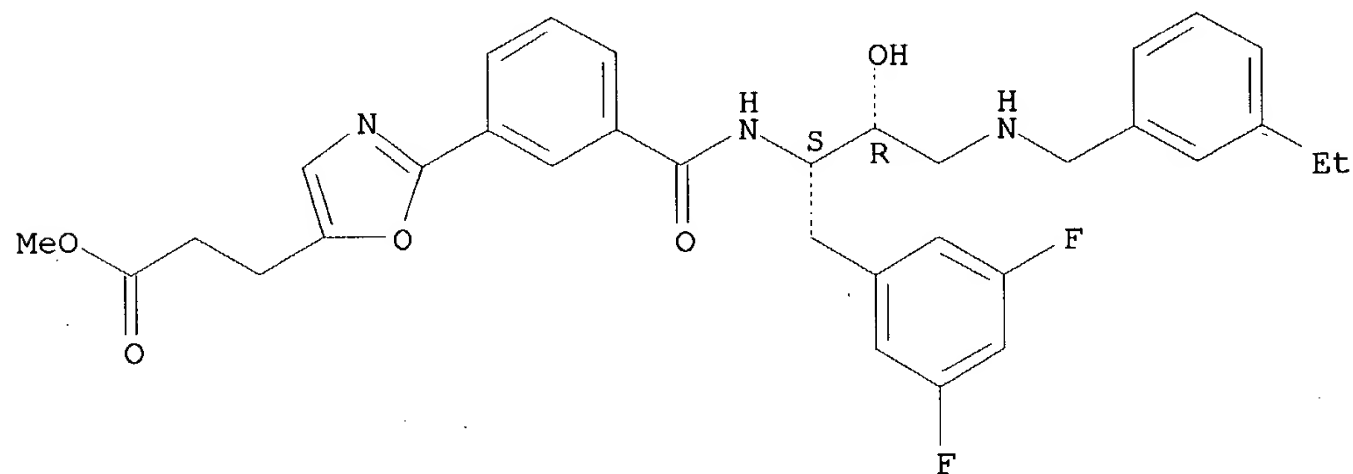
(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease)

09/895,871

RN 527728-59-2 CAPLUS

CN 5-Oxazolepropanoic acid, 2-[3-[[[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]amino]carbonyl]phenyl]-, methyl ester (9CI) (CA INDEX NAME)

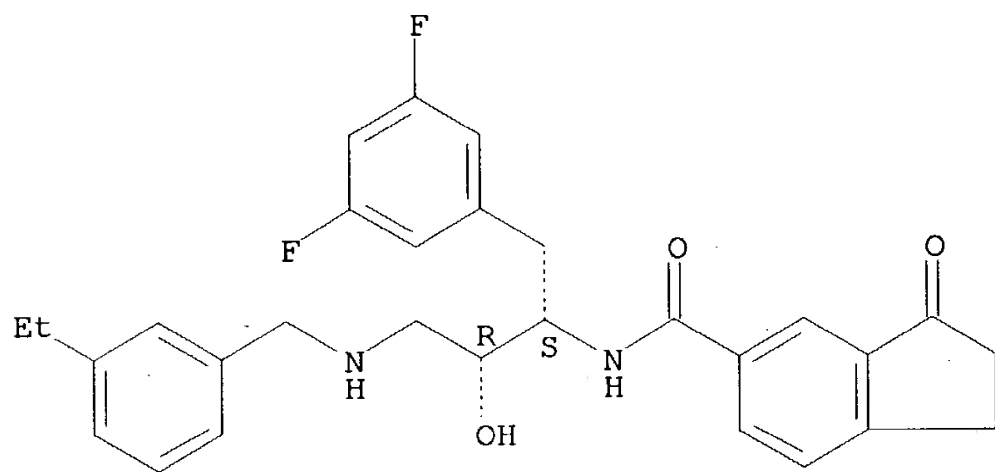
Absolute stereochemistry.



RN 527731-65-3 CAPLUS

CN 1H-Indene-5-carboxamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-2,3-dihydro-3-oxo- (9CI) (CA INDEX NAME)

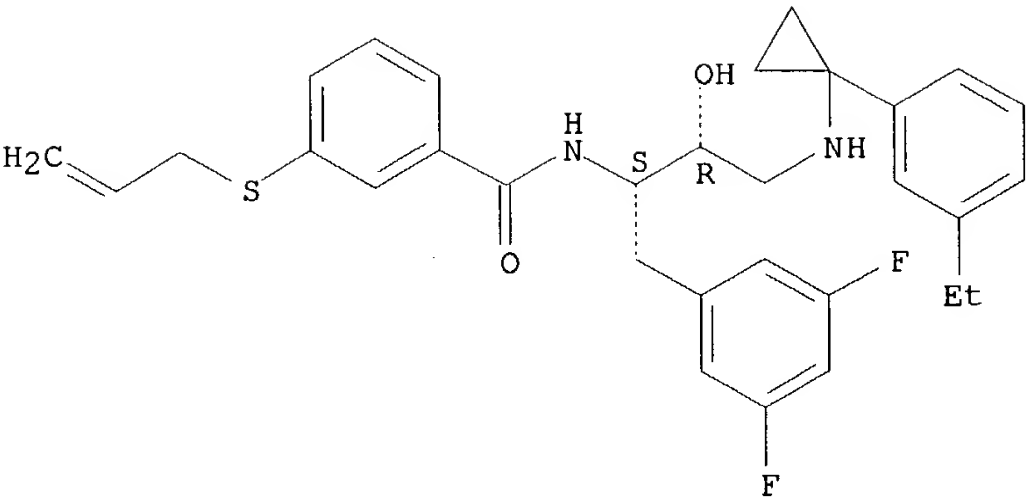
Absolute stereochemistry.



RN 527733-02-4 CAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[1-(3-ethylphenyl)cyclopropyl]amino]-2-hydroxypropyl]-3-(2-propenylthio)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT	388062-16-6P	388062-17-7P	388064-67-3P
	388064-70-8P	388064-96-8P	388065-05-2P
	388065-48-3P	388065-54-1P	388066-12-4P
	388066-14-6P	388066-16-8P	388066-17-9P
	388066-18-0P	388066-19-1P	388066-20-4P
	388066-21-5P	388066-25-9P	388066-26-0P
	388066-28-2P	388066-29-3P	388066-31-7P
	388066-32-8P	388066-39-5P	388066-40-8P
	388066-86-2P	388067-17-2P	388067-20-7P
	388067-23-0P	388067-43-4P	388067-75-2P
	388068-39-1P	388068-53-9P	388068-62-0P
	388068-68-6P	388068-70-0P	388068-85-7P
	388069-49-6P	388070-61-9P	388070-76-6P
	388070-80-2P	388071-79-2P	388071-81-6P
	388071-85-0P	388077-92-7P	527712-57-8P
	527712-59-0P	527712-61-4P	527712-62-5P
	527712-64-7P	527716-52-5P	527716-58-1P
	527716-59-2P	527716-60-5P	527716-61-6P
	527716-63-8P	527716-64-9P	527716-66-1P
	527716-67-2P	527716-68-3P	527716-70-7P
	527716-71-8P	527716-73-0P	527716-75-2P
	527716-77-4P	527716-78-5P	527716-79-6P
	527716-82-1P	527716-83-2P	527716-85-4P
	527716-86-5P	527716-87-6P	527716-90-1P
	527716-91-2P	527716-93-4P	527716-94-5P
	527716-96-7P	527716-97-8P	527716-99-0P
	527717-00-6P	527717-02-8P	527717-04-0P
	527717-06-2P	527717-08-4P	527717-10-8P
	527717-11-9P	527717-13-1P	527717-14-2P
	527717-16-4P	527717-17-5P	527717-21-1P
	527717-22-2P	527717-24-4P	527717-27-7P
	527717-29-9P	527717-30-2P	527717-31-3P
	527717-32-4P	527717-34-6P	527717-38-0P
	527717-39-1P	527717-42-6P	527717-45-9P
	527717-53-9P	527717-54-0P	527717-64-2P
	527717-73-3P	527717-74-4P	527717-84-6P
	527717-87-9P	527720-79-2P	527720-83-8P
	527721-90-0P	527724-43-2P	527726-37-0P
	527726-38-1P	527726-39-2P	527726-40-5P
	527726-41-6P	527726-42-7P	527726-45-0P
	527726-49-4P	527726-50-7P	527726-52-9P
	527726-53-0P	527726-54-1P	527726-55-2P
	527726-57-4P	527726-58-5P	527726-60-9P
	527726-62-1P	527726-63-2P	527726-66-5P
	527726-67-6P	527726-68-7P	527726-69-8P

527726-74-5P 527726-75-6P 527726-77-8P
 527726-78-9P 527726-79-0P 527726-80-3P
 527726-81-4P 527726-82-5P 527726-83-6P
 527726-85-8P 527726-86-9P 527726-87-0P
 527726-88-1P 527726-89-2P 527726-90-5P
 527726-91-6P 527726-92-7P 527726-93-8P
 527726-94-9P 527726-96-1P 527726-97-2P
 527726-99-4P 527727-01-1P 527727-02-2P
 527727-04-4P 527727-06-6P 527727-07-7P
 527727-08-8P 527727-09-9P 527727-10-2P
 527727-11-3P 527727-12-4P 527727-13-5P
 527727-14-6P 527727-15-7P 527727-16-8P
 527727-17-9P 527727-18-0P 527727-19-1P
 527727-20-4P 527727-21-5P 527727-22-6P
 527727-23-7P 527727-24-8P 527727-25-9P
 527727-26-0P 527727-27-1P 527727-29-3P
 527727-30-6P 527727-33-9P 527727-34-0P
 527727-35-1P 527727-36-2P 527727-41-9P
 527727-42-0P 527727-45-3P 527727-46-4P
 527727-47-5P 527727-48-6P 527727-57-7P
 527727-59-9P 527727-60-2P 527727-61-3P
 527727-62-4P 527727-63-5P 527727-64-6P
 527727-65-7P 527727-66-8P 527727-79-3P
 527727-80-6P 527727-81-7P 527727-82-8P
 527727-90-8P 527727-94-2P 527727-95-3P
 527727-98-6P 527727-99-7P 527728-03-6P
 527728-04-7P 527728-07-0P 527728-09-2P
 527728-11-6P 527728-13-8P 527728-14-9P
 527728-15-0P 527728-27-4P 527728-29-6P
 527728-30-9P 527728-32-1P 527728-33-2P
 527728-37-6P 527728-39-8P 527728-44-5P
 527728-49-0P 527728-53-6P 527728-54-7P
 527728-56-9P 527728-57-0P 527728-58-1P
 527728-60-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

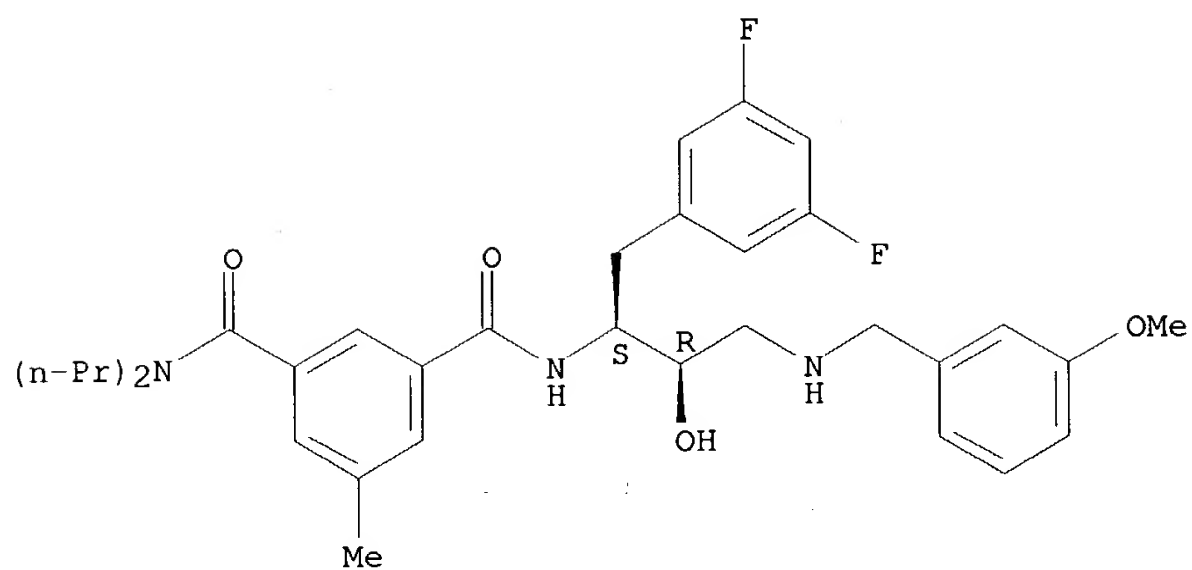
(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating
 Alzheimer's disease)

RN 388062-16-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-
 hydroxy-3-[[(3-methoxyphenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

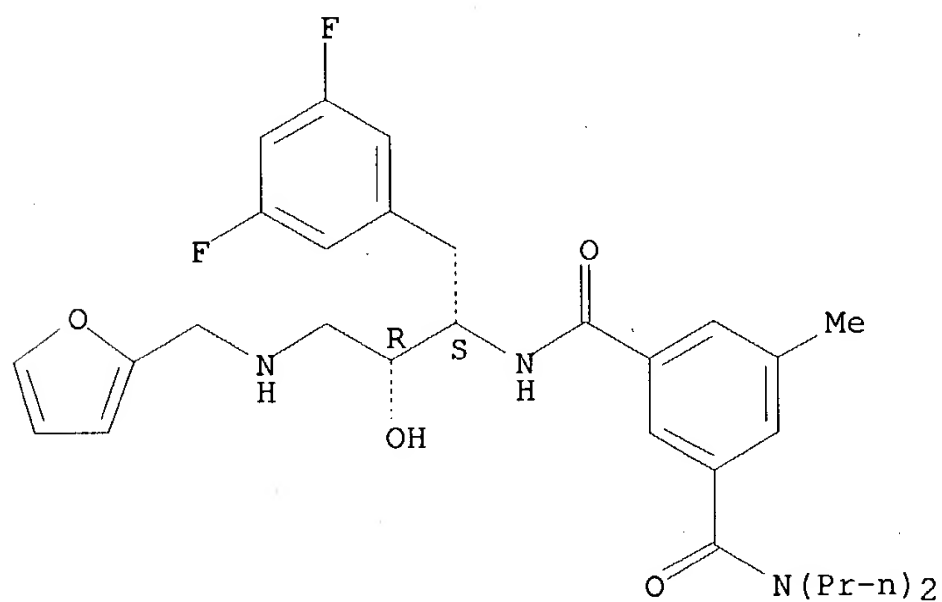
09/895,871



RN 388062-17-7 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[(2-furanylmethyl)amino]-2-hydroxypropyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

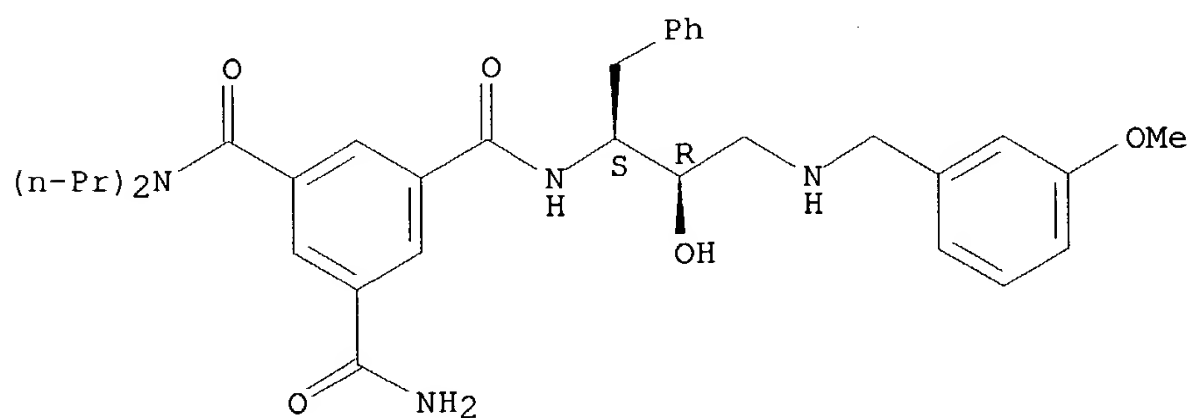
Absolute stereochemistry.



RN 388064-67-3 CAPLUS

CN 1,3,5-Benzenetricarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

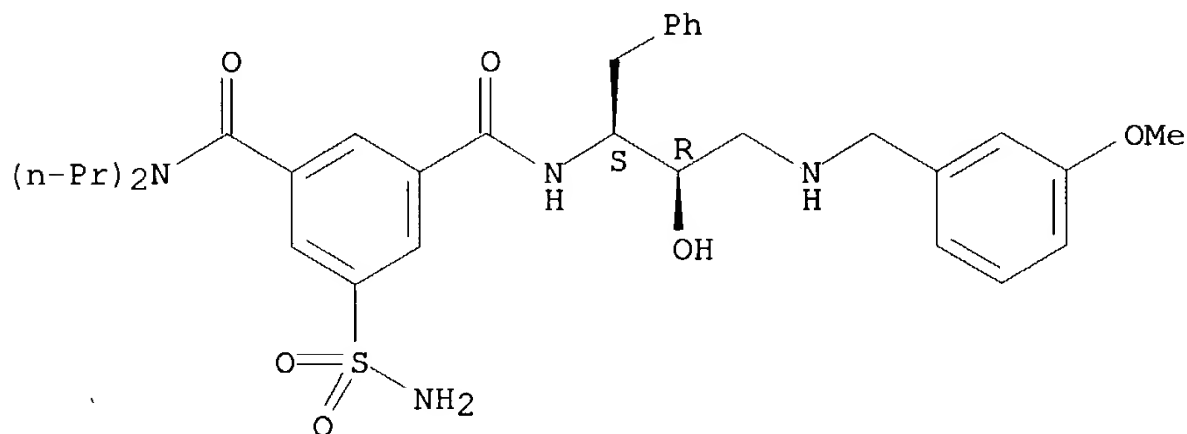


09/895,871

RN 388064-70-8 CAPLUS

CN 1,3-Benzenedicarboxamide, 5-(aminosulfonyl)-N'-[(1S,2R)-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI)
(CA INDEX NAME)

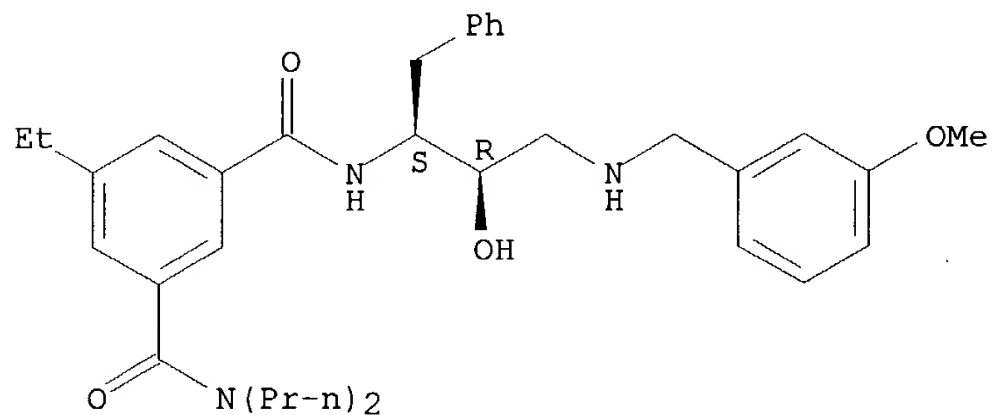
Absolute stereochemistry.



RN 388064-96-8 CAPLUS

CN 1,3-Benzenedicarboxamide, 5-ethyl-N'-[(1S,2R)-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

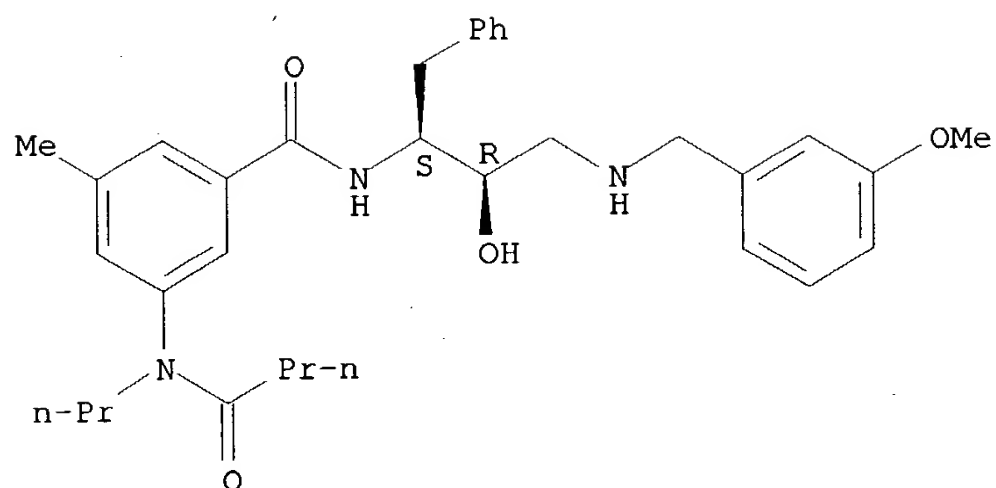


RN 388065-05-2 CAPLUS

CN Benzamide, N-[(1S,2R)-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-3-methyl-5-[(1-oxobutyl)propylamino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

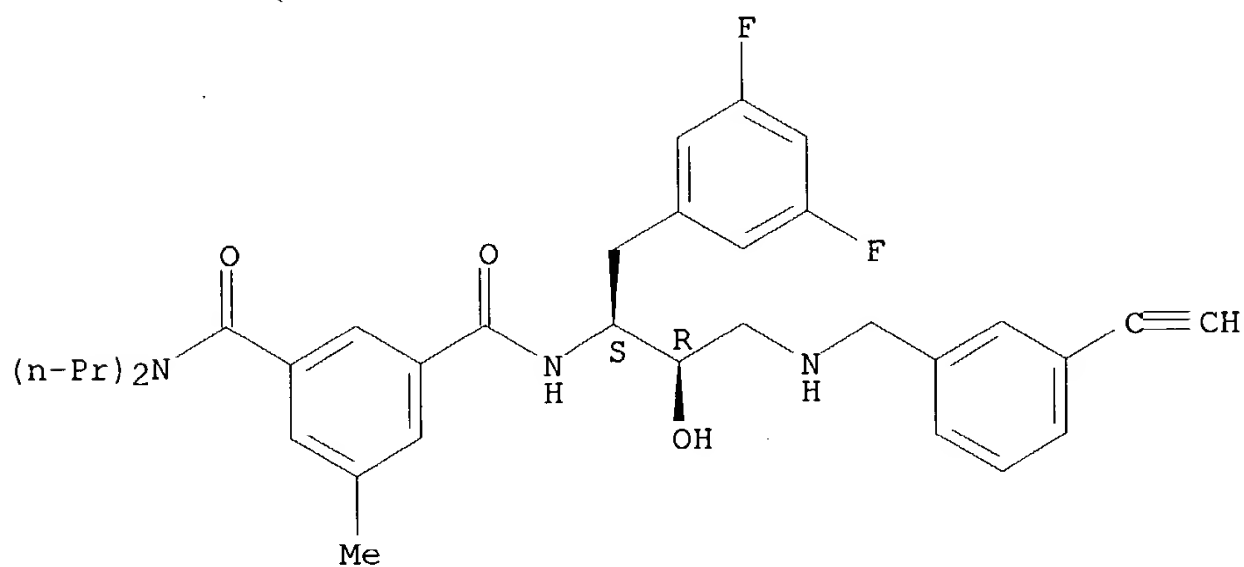
09/895,871



RN 388065-48-3 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethynylphenyl)methyl]amino]-2-hydroxypropyl]-5-methyl-N,N-dipropyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 388065-54-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-ethynyl-N,N-dipropyl-
(9CI) (CA INDEX NAME)

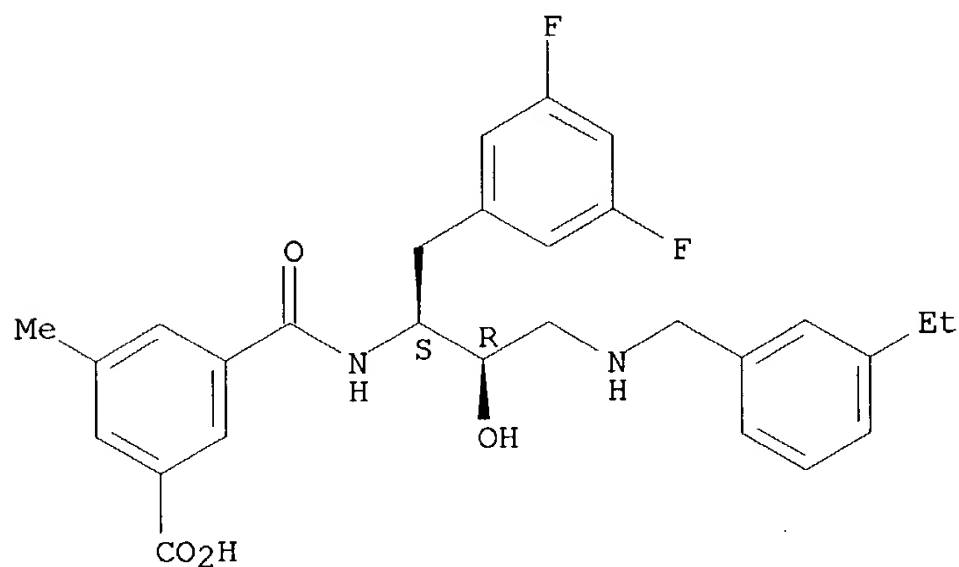
Absolute stereochemistry.

09/895,871

RN 597562-97-5 CAPLUS

CN Benzoic acid, 3-[[[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]amino]carbonyl]-5-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

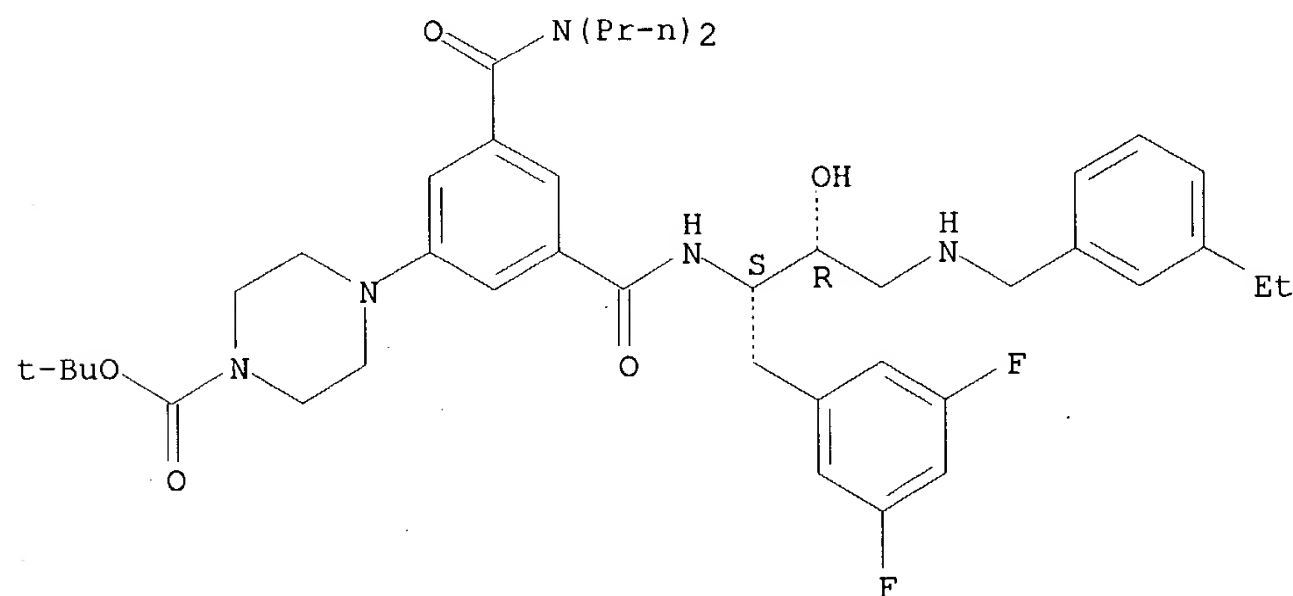


● HCl

RN 597563-70-7 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[3-[[[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]amino]carbonyl]-5-[(dipropylamino)carbonyl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:376819 CAPLUS

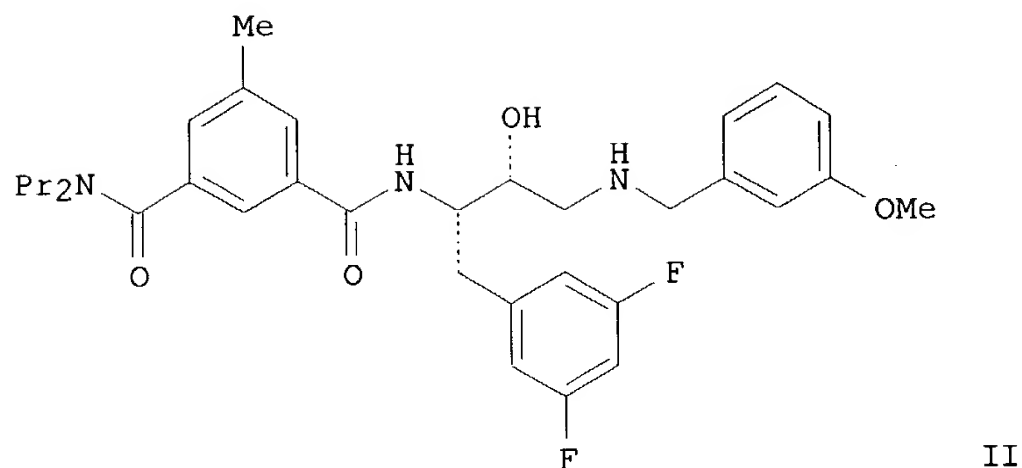
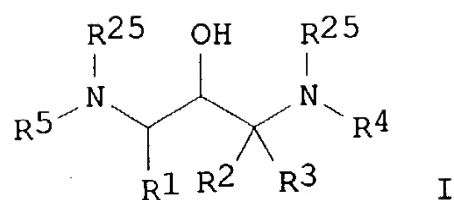
DOCUMENT NUMBER: 138:385173

TITLE: Preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease

09/895,871

INVENTOR(S): Varghese, John; Maillard, Michel; Jagodzinska, Barbara; Beck, James P.; Gailunas, Andrea; Fang, Larry; Sealy, Jennifer; Tenbrink, Ruth; Freskos, John; Mickelson, John; Samala, Lakshman; Hom, Roy
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company
SOURCE: PCT Int. Appl., 1243 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040096	A2	20030515	WO 2002-US36072	20021108
WO 2003040096	A3	20040506		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
WO 2003040096	A2	20030515	WO 2002-XA36072	20021108
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004171881	A1	20040902	US 2002-291318	20021108
EP 1453789	A2	20040908	EP 2002-793909	20021108
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
PRIORITY APPLN. INFO.:			US 2001-337122P	P 20011108
			US 2001-344086P	P 20011228
			US 2002-345635P	P 20020103
			WO 2002-US36072	A 20021108
OTHER SOURCE(S):	MARPAT 138:385173			
GI				



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, alkyl, haloalkyl, alkenyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; or R2 and R3 are taken together with the carbon to which they are attached to form a carbocycle of 3-7 carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of O, S, SO₂, (un)substituted NH; R4 = alkyl, haloalkyl, hydroxyalkyl, etc.; R5 = R6X (wherein X = CO, SO₂, (un)substituted CH₂; R6 = (un)substituted Ph, naphthyl, indanyl, etc.); R25 = H, alkyl, alkoxy, etc.] which have activity as inhibitors of β -secretase and are therefore useful in treating a variety of disorders such as Alzheimer's disease, were prepared E.g., a multi-step synthesis of (1S,2R)-II, starting from (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5-difluorophenyl)propanoic acid, was given. The compds. I showed IC₅₀ of < 20 μ M in cell free inhibition assay utilizing a synthetic APP substrate. This is a Part 1 of 1-2 series.

IT 388063-45-4P 388063-51-2P 388063-56-7P
 388063-57-8P 388064-22-0P 388064-34-4P
 388064-46-8P 388065-31-4P 388065-36-9P
 388065-51-8P 388065-54-1P 388065-60-9P
 388065-84-7P 388065-87-0P 388066-79-3P
 388066-86-2P 388066-92-0P 388066-94-2P
 388066-96-4P 388066-98-6P 388066-99-7P
 388067-00-3P 388067-02-5P 388067-03-6P
 388067-04-7P 388067-06-9P 388067-07-0P
 388067-09-2P 388067-11-6P 388067-12-7P
 388067-13-8P 388067-15-0P 388067-16-1P
 388067-17-2P 388067-20-7P 388067-28-5P
 388067-42-3P 388067-43-4P 388067-54-7P
 388067-57-0P 388067-61-6P 388067-64-9P
 388067-67-2P 388067-72-9P 388067-73-0P
 388067-75-2P 388067-78-5P 388067-80-9P
 388067-84-3P 388067-96-7P 388068-39-1P
 388068-53-9P 388068-62-0P 388068-68-6P
 388068-70-0P 388068-85-7P 388069-13-4P
 388069-15-6P 388069-28-1P 388069-43-0P
 388069-45-2P 388069-57-6P 388070-61-9P

388070-76-6P 388070-80-2P 388071-06-5P
388072-21-7P 388077-92-7P 388569-65-1P
527712-34-1P 527712-36-3P 527712-38-5P
527712-39-6P 527712-41-0P 527712-43-2P
527712-45-4P 527712-47-6P 527712-49-8P
527712-51-2P 527712-57-8P 527712-59-0P
527712-61-4P 527712-62-5P 527712-64-7P
527712-68-1P 527713-57-1P 527714-31-4P
527714-35-8P 527714-62-1P 527715-26-0P
527715-28-2P 527715-30-6P 527715-54-4P
527715-56-6P 527715-58-8P 527715-62-4P
527715-83-9P 527715-85-1P 527715-89-5P
527716-17-2P 527716-28-5P 527716-42-3P
527716-50-3P 527716-52-5P 527716-54-7P
527716-56-9P 527716-58-1P 527716-59-2P
527716-60-5P 527716-61-6P 527716-62-7P
527716-63-8P 527716-64-9P 527716-66-1P
527716-67-2P 527716-68-3P 527716-69-4P
527716-70-7P 527716-71-8P 527716-72-9P
527716-73-0P 527716-74-1P 527716-75-2P
527716-76-3P 527716-77-4P 527716-78-5P
527716-79-6P 527716-80-9P 527716-81-0P
527716-82-1P 527716-83-2P 527716-84-3P
527716-85-4P 527716-86-5P 527716-87-6P
527716-88-7P 527716-89-8P 527716-90-1P
527716-91-2P 527716-93-4P 527716-94-5P
527716-95-6P 527716-96-7P 527716-97-8P
527716-99-0P 527717-00-6P 527717-02-8P
527717-03-9P 527717-04-0P 527717-05-1P
527717-06-2P 527717-07-3P 527717-08-4P
527717-09-5P 527717-10-8P 527717-11-9P
527717-13-1P 527717-14-2P 527717-15-3P
527717-16-4P 527717-17-5P 527717-20-0P
527717-21-1P 527717-22-2P 527717-24-4P
527717-25-5P 527717-26-6P 527717-27-7P
527717-28-8P 527717-29-9P 527717-30-2P
527717-31-3P 527717-32-4P 527717-33-5P
527717-34-6P 527717-36-8P 527717-38-0P
527717-39-1P 527717-40-4P 527717-42-6P
527717-45-9P 527717-47-1P 527717-50-6P
527717-51-7P 527717-53-9P 527717-54-0P
527717-55-1P 527717-56-2P 527717-58-4P
527717-63-1P 527717-64-2P 527717-66-4P
527717-73-3P 527717-74-4P 527717-75-5P
527717-76-6P 527717-77-7P 527717-78-8P
527717-79-9P 527717-80-2P 527717-81-3P
527717-82-4P 527717-84-6P 527717-85-7P
527717-87-9P 527717-96-0P 527717-97-1P
527718-03-2P 527718-07-6P 527718-10-1P
527718-14-5P 527718-15-6P 527718-16-7P
527718-17-8P 527718-18-9P 527718-25-8P
527718-28-1P 527718-33-8P 527718-34-9P
527718-37-2P 527718-43-0P 527718-44-1P
527718-45-2P 527718-47-4P 527718-48-5P
527718-49-6P 527718-56-5P 527718-60-1P
527718-62-3P 527718-64-5P 527718-65-6P
527718-66-7P 527718-73-6P 527718-79-2P
527718-81-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

09/895,871

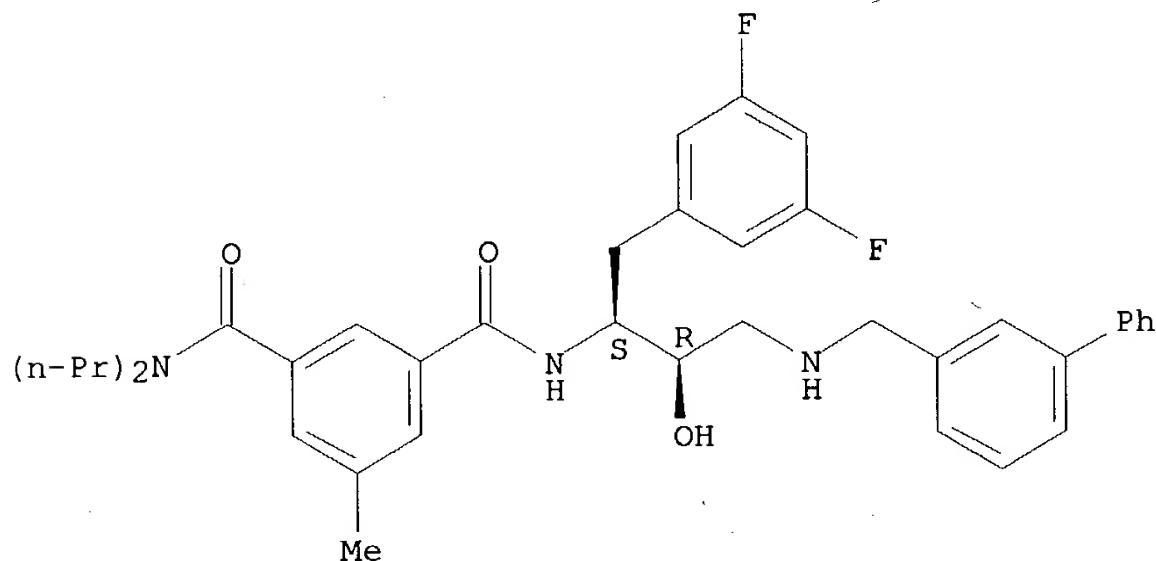
(Uses)

(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease)

RN 388063-45-4 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-[[[1,1'-biphenyl]-3-ylmethyl)amino]-1-[(3,5-difluorophenyl)methyl]-2-hydroxypropyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

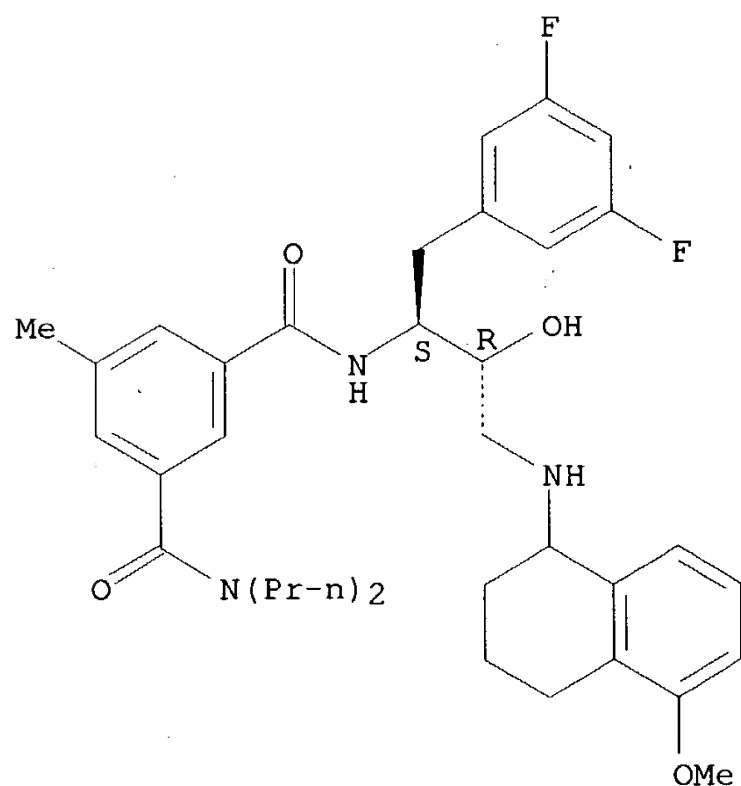
Absolute stereochemistry.



RN 388063-51-2 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[(1,2,3,4-tetrahydro-5-methoxy-1-naphthalenyl)amino]propyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



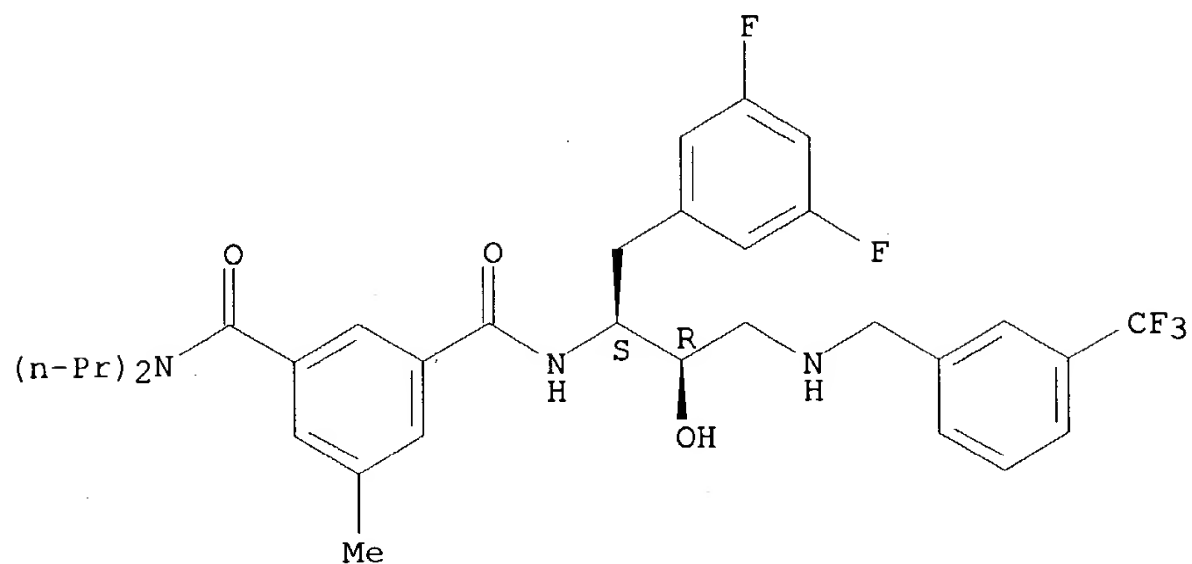
RN 388063-56-7 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[[3-(trifluoromethyl)phenyl]methyl]amino]propyl]-5-methyl-N,N-

09/895,871

dipropyl- (9CI) (CA INDEX NAME)

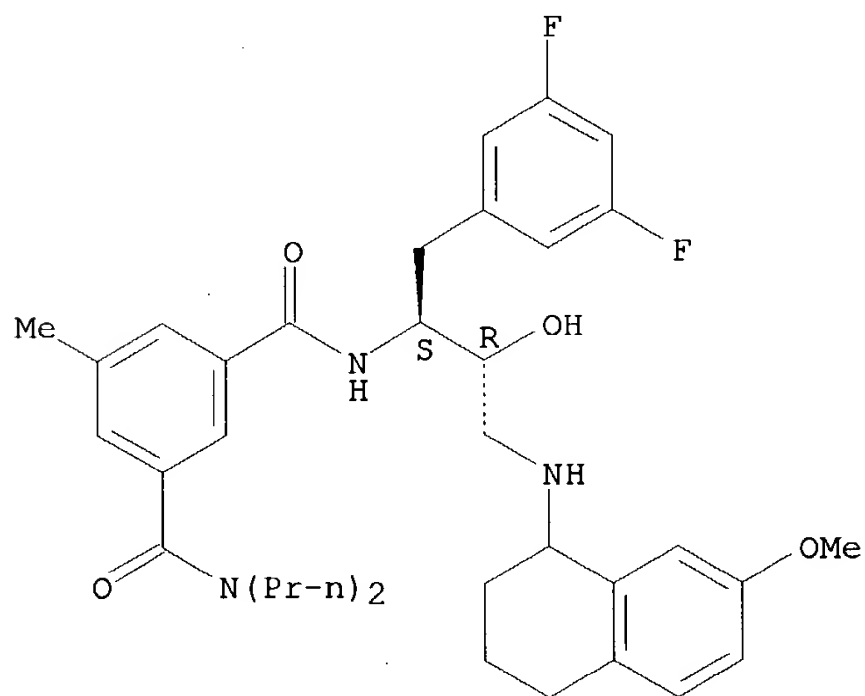
Absolute stereochemistry.



RN 388063-57-8 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[(1,2,3,4-tetrahydro-7-methoxy-1-naphthalenyl)amino]propyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

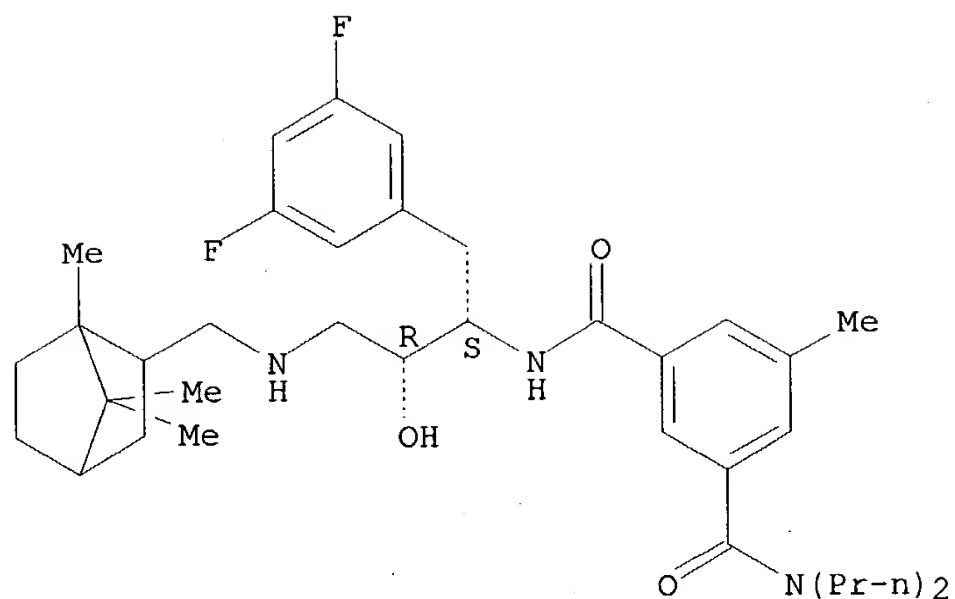


RN 388064-22-0 CAPLUS

CN 2-Anthracenecarboxamide, 9,10-dihydro-N-[(1S,2R)-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-9,10-dioxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

09/895,871



L5 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:832774 CAPLUS

DOCUMENT NUMBER: 137:325641

TITLE: Processes for the synthesis of amino acid-related
benzyl epoxides used in the production of
pharmaceutical agents

INVENTOR(S): Reeder, Michael R.

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn
Company

SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085877	A2	20021031	WO 2002-US12591	20020423
WO 2002085877	A3	20030306		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2003004360	A1	20030102	US 2002-128122	20020423
EP 1381597	A2	20040121	EP 2002-728882	20020423
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
BR 2002009163	A	20040824	BR 2002-9163	20020423
JP 2004529152	T2	20040924	JP 2002-583404	20020423
NO 2003004738	A	20031204	NO 2003-4738	20031023
ZA 2003008261	A	20040524	ZA 2003-8261	20031023
PRIORITY APPLN. INFO.:			US 2001-285772P	P 20010423
			WO 2002-US12591	W 20020423

OTHER SOURCE(S): CASREACT 137:325641; MARPAT 137:325641

09/895,871

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides amino acids $R_3NHCH(CH_2R)CO_2R_1$ [R = (un)substituted phenyl; R_1 = allyl or (un)substituted alkyl, Ph, or benzyl; R_3 = H or a protecting group], amino alcs. $H_2NCH(CH_2R)CH(OH)CH_2R_2$ [R_2 = Cl, Br, trialkylsilyl, or tri-substituted aminosilyl], corresponding epoxides, and other intermediates used in the production of pharmaceutical agents. Thus, Boc-protected 3,5-difluoro-L-phenylalanine underwent sequential Me esterification, reaction with $ClCH_2I$, borohydride reduction, and conversion to epoxide I (KOH/EtOH). Ring opening of I with 3-methoxybenzylamine, deprotection, and acylation with 5-methyl-N,N-dipropylisophthalamide afforded amino alc. derivative II.

IT **388062-16-6P**

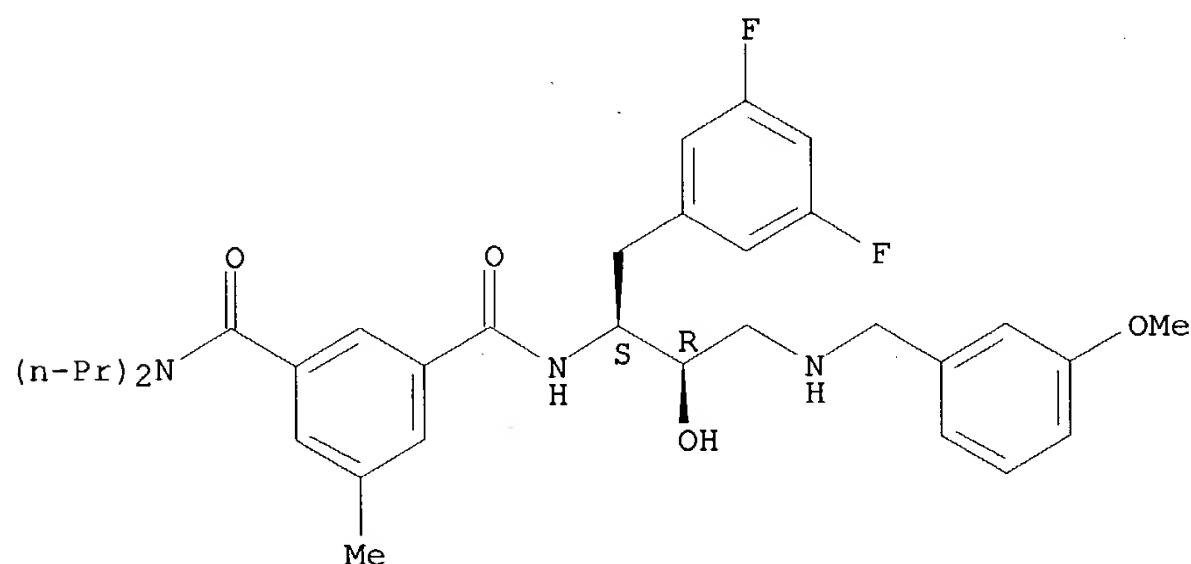
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis of amino acid-related benzyl epoxides for production of pharmaceuticals)

RN 388062-16-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[(3-methoxyphenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:31402 CAPLUS

DOCUMENT NUMBER: 136:102190

TITLE: Preparation of substituted amines to treat Alzheimer's disease

INVENTOR(S): Maillaird, Michel; Hom, Court; Gailunas, Andrea; Jagodzinska, Barbara; Fang, Lawrence Y.; John, Varghese; Freskos, John N.; Pulley, Shon R.; Beck, James P.; Tenbrink, Ruth E.

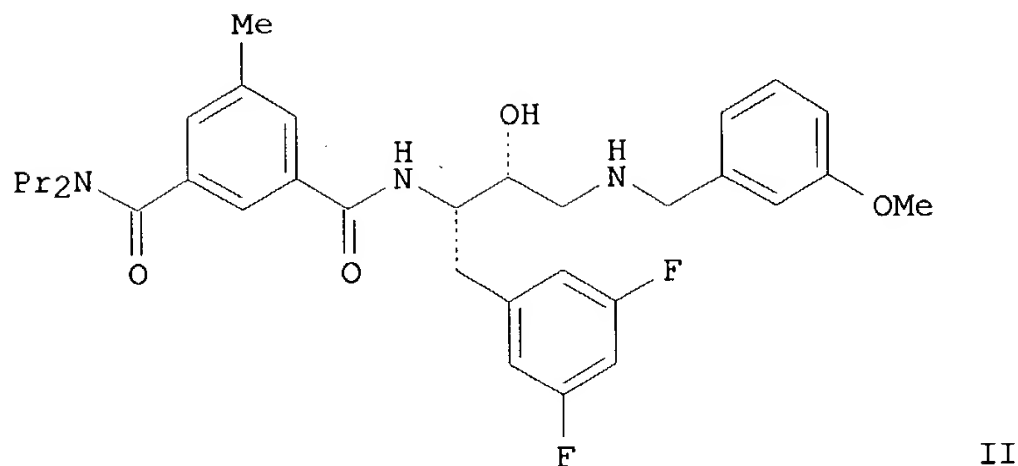
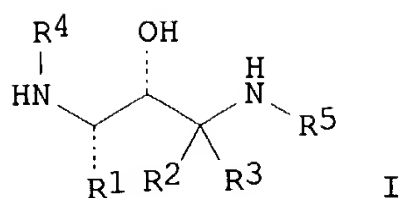
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company

SOURCE: PCT Int. Appl., 651 pp.
CODEN: PIXXD2

09/895,871

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002512	A2	20020110	WO 2001-US21012	20010629
WO 2002002512	A3	20030821		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2410651	AA	20020110	CA 2001-2410651	20010629
AU 2001073137	A5	20020114	AU 2001-73137	20010629
US 2002128255	A1	20020912	US 2001-896139	20010629
BR 2001012000	A	20030603	BR 2001-12000	20010629
EP 1353898	A2	20031022	EP 2001-952378	20010629
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004502669	T2	20040129	JP 2002-507769	20010629
EE 200200716	A	20040816	EE 2002-716	20010629
NO 2002006199	A	20030221	NO 2002-6199	20021223
PRIORITY APPLN. INFO.:			US 2000-215323P	P 20000630
			US 2000-252736P	P 20001122
			US 2000-255956P	P 20001215
			US 2001-268497P	P 20010213
			US 2001-279779P	P 20010329
			US 2001-295589P	P 20010604
			WO 2001-US21012	W 20010629
OTHER SOURCE(S):	MARPAT 136:102190			
GI				



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, (un)substituted alkyl, alkenyl, etc.; R3 = H, (un)substituted alkyl, alkenyl, etc.; R4 = XR; X = CO, SO₂, a bond, etc.; R = Ph, naphthyl, indanyl, etc.; R5 = (un)substituted alkyl, (CH₂)₀₋₃cycloalkyl, etc.], useful in treating Alzheimer's disease and other similar diseases, were prepared Thus, reacting (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol trifluoroacetate with 5-methyl-N,N-dipropylisophthalamide in the presence of Et₃N, 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in DMF afforded (1S,2R)-II. The compds. I exhibit an IC₅₀ of < 50 μM against beta-secretase.

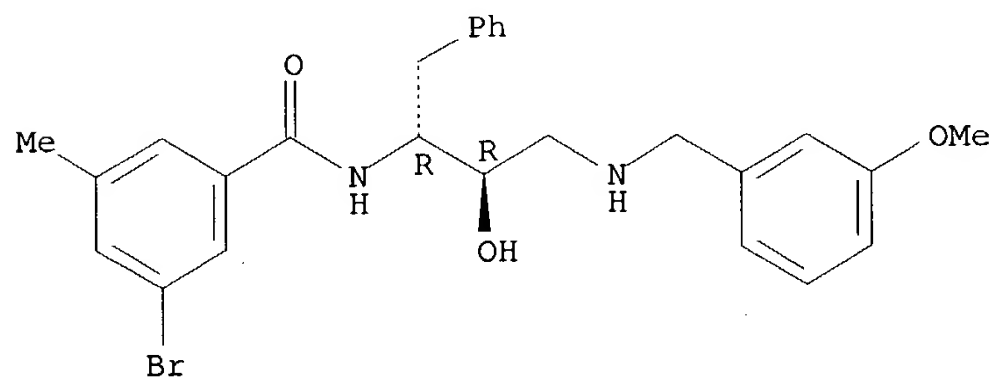
IT **388066-36-2P**

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of substituted amines for treating Alzheimer's disease)

RN 388066-36-2 CAPLUS

CN Benzamide, 3-bromo-N-[(1R,2R)-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **388062-16-6P 388062-17-7P 388062-19-9P**
388062-21-3P 388062-22-4P 388062-23-5P

388062-26-8P 388062-27-9P 388062-29-1P
388062-31-5P 388062-34-8P 388062-35-9P
388062-36-0P 388062-37-1P 388062-38-2P
388062-43-9P 388062-48-4P 388062-49-5P
388062-50-8P 388062-51-9P 388062-52-0P
388062-53-1P 388062-54-2P 388062-56-4P
388062-57-5P 388062-58-6P 388062-59-7P
388062-60-0P 388062-61-1P 388062-62-2P
388062-63-3P 388062-64-4P 388062-65-5P
388062-66-6P 388062-67-7P 388062-68-8P
388062-69-9P 388062-70-2P 388062-71-3P
388062-72-4P 388062-73-5P 388062-74-6P
388062-75-7P 388062-78-0P 388062-79-1P
388062-82-6P 388062-83-7P 388062-88-2P
388062-89-3P 388062-90-6P 388062-91-7P
388062-92-8P 388062-93-9P 388062-94-0P
388062-95-1P 388062-96-2P 388062-98-4P
388063-00-1P 388063-02-3P 388063-05-6P
388063-07-8P 388063-09-0P 388063-10-3P
388063-18-1P 388063-22-7P 388063-26-1P
388063-32-9P 388063-38-5P 388063-43-2P
388063-44-3P 388063-45-4P 388063-46-5P
388063-47-6P 388063-49-8P 388063-50-1P
388063-51-2P 388063-52-3P 388063-53-4P
388063-54-5P 388063-55-6P 388063-56-7P
388063-57-8P 388063-58-9P 388063-59-0P
388063-60-3P 388063-61-4P 388063-62-5P
388063-63-6P 388063-64-7P 388063-65-8P
388063-66-9P 388063-68-1P 388063-72-7P
388063-73-8P 388063-78-3P 388063-80-7P
388063-81-8P 388063-82-9P 388063-83-0P
388063-84-1P 388063-85-2P 388063-86-3P
388063-87-4P 388063-88-5P 388063-89-6P
388063-90-9P 388063-91-0P 388063-92-1P
388063-93-2P 388063-94-3P 388063-95-4P
388063-96-5P 388063-97-6P 388063-98-7P
388063-99-8P 388064-00-4P 388064-01-5P
388064-02-6P 388064-03-7P 388064-05-9P
388064-06-0P 388064-07-1P 388064-13-9P
388064-14-0P 388064-15-1P 388064-16-2P
388064-17-3P 388064-18-4P 388064-19-5P
388064-20-8P 388064-21-9P 388064-22-0P
388064-23-1P 388064-24-2P 388064-25-3P
388064-26-4P 388064-27-5P 388064-28-6P
388064-29-7P 388064-30-0P 388064-31-1P
388064-32-2P 388064-33-3P 388064-34-4P
388064-35-5P 388064-36-6P 388064-37-7P
388064-38-8P 388064-39-9P 388064-40-2P
388064-41-3P 388064-42-4P 388064-43-5P
388064-44-6P 388064-46-8P 388064-47-9P
388064-48-0P 388064-49-1P 388064-50-4P
388064-51-5P 388064-53-7P 388064-55-9P
388064-56-0P 388064-57-1P 388064-58-2P
388064-59-3P 388064-60-6P 388064-61-7P
388064-62-8P 388064-65-1P 388064-66-2P
388064-67-3P 388064-70-8P 388064-71-9P
388064-72-0P 388064-73-1P 388064-96-8P
388064-97-9P 388064-98-0P 388064-99-1P
388065-00-7P 388065-01-8P 388065-04-1P
388065-05-2P 388065-06-3P 388065-07-4P

09/895,871

388065-08-5P 388065-09-6P 388065-13-2P
388065-14-3P 388065-15-4P 388065-16-5P
388065-19-8P 388065-20-1P 388065-21-2P
388065-22-3P 388065-23-4P 388065-24-5P
388065-27-8P 388065-29-0P 388065-30-3P
388065-31-4P 388065-33-6P 388065-36-9P
388065-37-0P 388065-39-2P 388065-42-7P
388065-43-8P 388065-44-9P 388065-47-2P
388065-48-3P 388065-49-4P 388065-50-7P
388065-51-8P 388065-52-9P 388065-54-1P
388065-59-6P 388065-60-9P 388065-62-1P
388065-63-2P 388065-64-3P 388065-65-4P
388065-66-5P 388065-67-6P 388065-68-7P
388065-70-1P 388065-72-3P 388065-73-4P
388065-74-5P 388065-75-6P 388065-78-9P
388065-79-0P 388065-80-3P 388065-81-4P
388065-82-5P

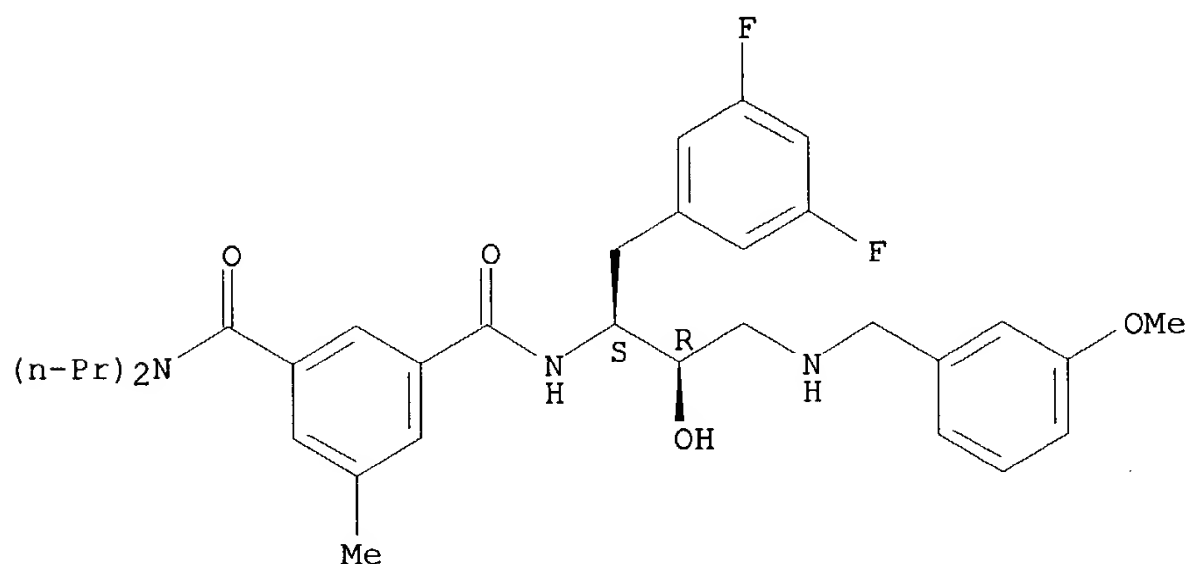
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of substituted amines for treating Alzheimer's disease)

RN 388062-16-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-
hydroxy-3-[[(3-methoxyphenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 388062-17-7 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[(2-
furanylmethyl)amino]-2-hydroxypropyl]-5-methyl-N,N-dipropyl- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

09/895,871

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

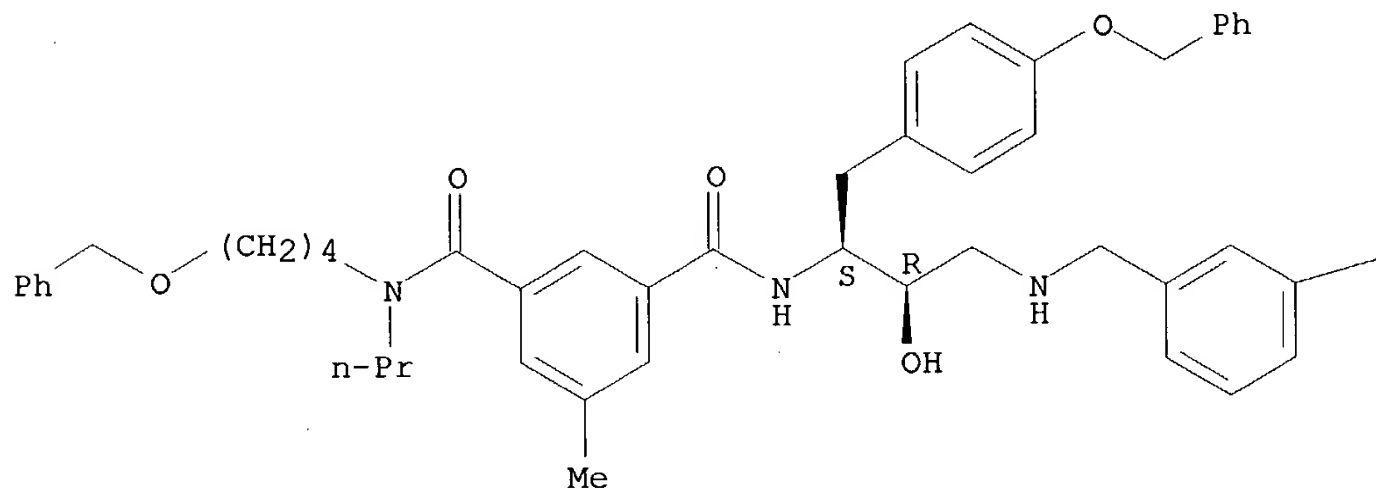
(preparation of substituted amines for treating Alzheimer's disease)

RN 388071-98-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[[3-methoxyphenyl)methyl]amino]-1-[[4-(phenylmethoxy)phenyl)methyl]propyl]-5-methyl-N-[4-(phenylmethoxy)butyl]-N-propyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

—OMe

L5 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:31396 CAPLUS
DOCUMENT NUMBER: 136:102189
TITLE: Preparation of substituted amines for treating Alzheimer's disease
INVENTOR(S): Fang, Lawrence Y.; Hom, Roy; John, Varghese; Maillaird, Michel
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002505	A2	20020110	WO 2001-US20852	20010629
WO 2002002505	A3	20020801		
WO 2002002505	C1	20031120		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

09/895,871

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,
VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG,
KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,
IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
GW, ML, MR, NE, SN, TD, TG

CA 2410680	AA	20020110	CA 2001-2410680	20010629
US 2002016320	A1	20020207	US 2001-896874	20010629
EP 1299349	A2	20030409	EP 2001-950719	20010629

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 2003096864	A1	20030522	US 2001-895871	20010629
JP 2004502664	T2	20040129	JP 2002-507762	20010629
ZA 2002009991	A	20040503	ZA 2002-9991	20021210
ZA 2003000327	A	20040325	ZA 2003-327	20030113

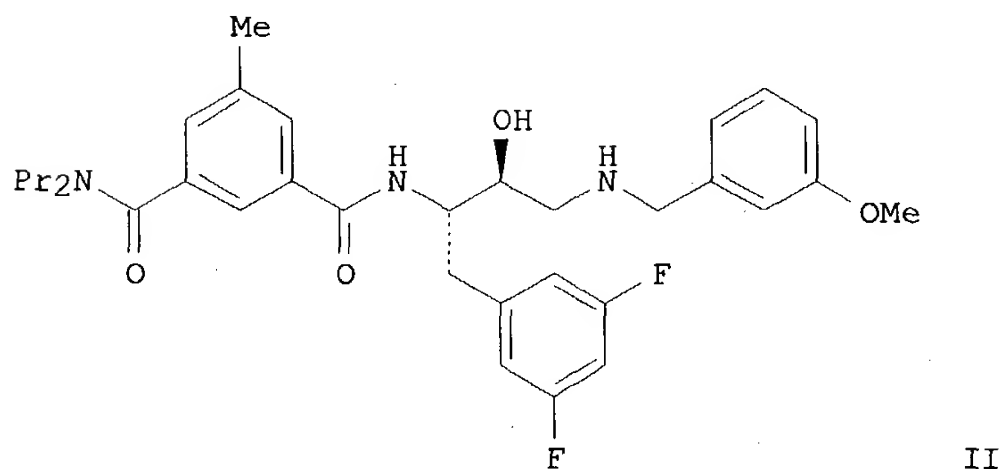
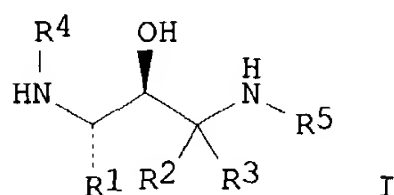
PRIORITY APPLN. INFO.:

US 2000-215323P	P	20000630
WO 2001-US20852	W	20010629

OTHER SOURCE(S):

MARPAT 136:102189

GI



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, (un)substituted alkyl; R3 = H, (un)substituted alkyl; or R2 and R3 are taken together with the carbon to which they are attached to form (un)substituted 3-7 membered carbo(or hetero)cycle; R4 = RX; X = CO, SO2; R = Ph, naphthyl, indanyl, etc.; R5 = alkyl, (CH2)0-3cycloalkyl, etc.], useful as β -secretase inhibitors, were prepared Thus, reacting (2S,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol trifluoroacetate with N,N,-dipropylamidoisophthalic acid in the presence of Et3N, HOBt and EDC in CH2Cl2 afforded (1S,2S)-II.

IT 388077-90-5P 388077-92-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

09/895,871

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides amino acids $R_3NHCH(CH_2R)CO_2R_1$ [R = (un)substituted phenyl; R_1 = allyl or (un)substituted alkyl, Ph, or benzyl; R_3 = H or a protecting group], amino alcs. $H_2NCH(CH_2R)CH(OH)CH_2R_2$ [R_2 = Cl, Br, trialkylsilyl, or tri-substituted aminosilyl], corresponding epoxides, and other intermediates used in the production of pharmaceutical agents. Thus, Boc-protected 3,5-difluoro-L-phenylalanine underwent sequential Me esterification, reaction with $ClCH_2I$, borohydride reduction, and conversion to epoxide I (KOH/EtOH). Ring opening of I with 3-methoxybenzylamine, deprotection, and acylation with 5-methyl-N,N-dipropylisophthalamide afforded amino alc. derivative II.

IT **388062-16-6P**

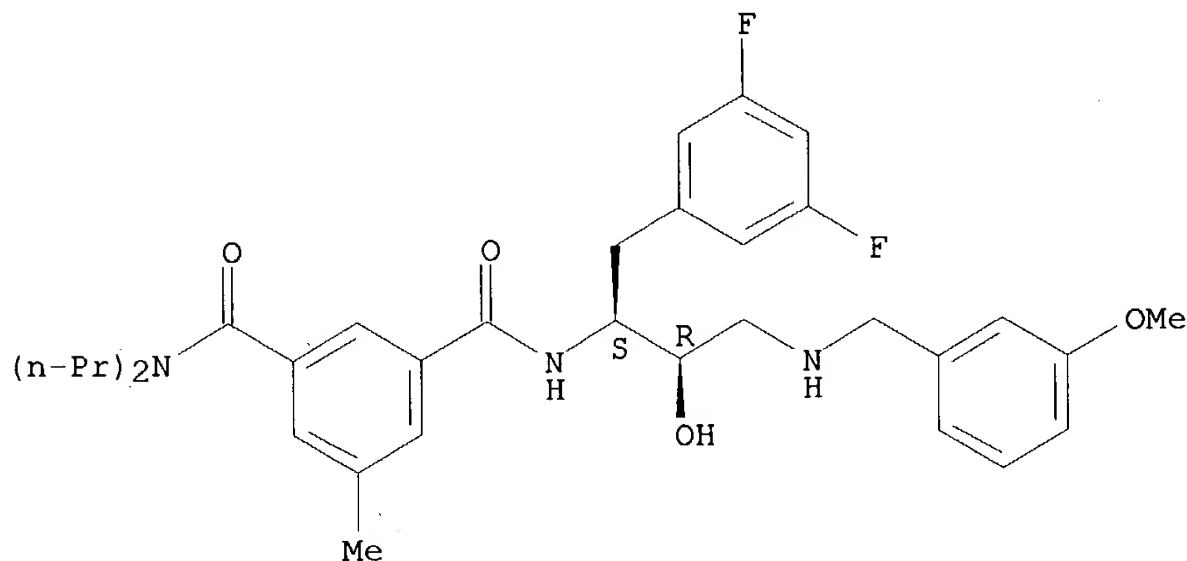
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis of amino acid-related benzyl epoxides for production of pharmaceuticals)

RN 388062-16-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:31402 CAPLUS

DOCUMENT NUMBER: 136:102190

TITLE: Preparation of substituted amines to treat Alzheimer's disease

INVENTOR(S): Maillaird, Michel; Hom, Court; Gailunas, Andrea; Jagodzinska, Barbara; Fang, Lawrence Y.; John, Varghese; Freskos, John N.; Pulley, Shon R.; Beck, James P.; Tenbrink, Ruth E.

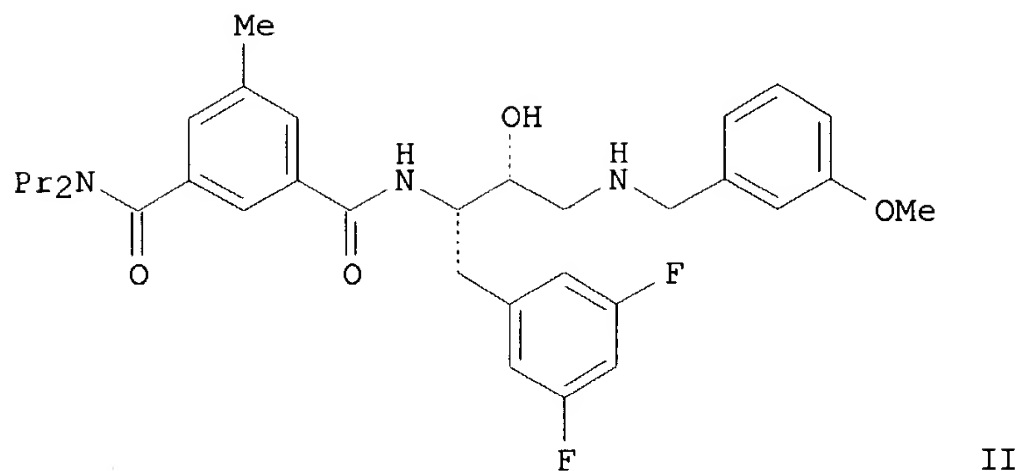
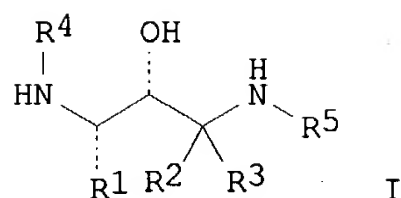
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company

SOURCE: PCT Int. Appl., 651 pp.
CODEN: PIXXD2

09/895,871

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002512	A2	20020110	WO 2001-US21012	20010629
WO 2002002512	A3	20030821		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2410651	AA	20020110	CA 2001-2410651	20010629
AU 2001073137	A5	20020114	AU 2001-73137	20010629
US 2002128255	A1	20020912	US 2001-896139	20010629
BR 2001012000	A	20030603	BR 2001-12000	20010629
EP 1353898	A2	20031022	EP 2001-952378	20010629
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004502669	T2	20040129	JP 2002-507769	20010629
EE 200200716	A	20040816	EE 2002-716	20010629
NO 2002006199	A	20030221	NO 2002-6199	20021223
PRIORITY APPLN. INFO.:			US 2000-215323P	P 20000630
			US 2000-252736P	P 20001122
			US 2000-255956P	P 20001215
			US 2001-268497P	P 20010213
			US 2001-279779P	P 20010329
			US 2001-295589P	P 20010604
			WO 2001-US21012	W 20010629
OTHER SOURCE(S):	MARPAT 136:102190			
GI				



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, (un)substituted alkyl, alkenyl, etc.; R3 = H, (un)substituted alkyl, alkenyl, etc.; R4 = XR; X = CO, SO₂, a bond, etc.; R = Ph, naphthyl, indanyl, etc.; R5 = (un)substituted alkyl, (CH₂)₀₋₃cycloalkyl, etc.], useful in treating Alzheimer's disease and other similar diseases, were prepared. Thus, reacting (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol trifluoroacetate with 5-methyl-N,N-dipropylisophthalamide in the presence of Et₃N, 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in DMF afforded (1S,2R)-II. The compds. I exhibit an IC₅₀ of < 50 μM against beta-secretase.

IT **388066-36-2P**

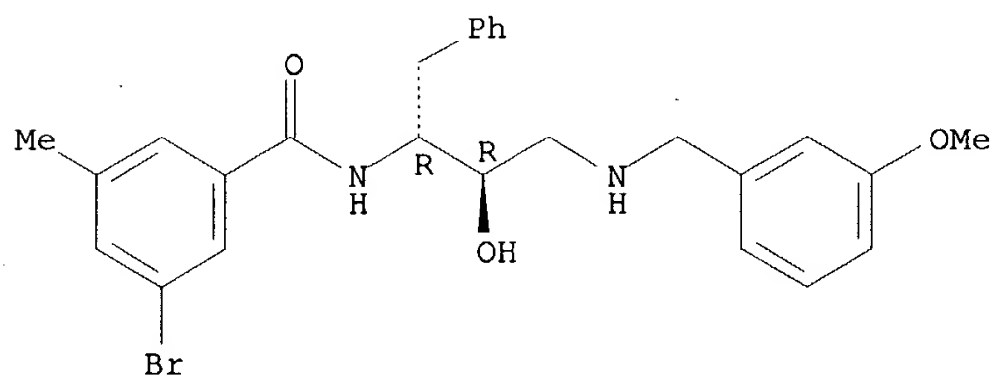
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of substituted amines for treating Alzheimer's disease)

RN 388066-36-2 CAPLUS

CN Benzamide, 3-bromo-N-[(1R,2R)-2-hydroxy-3-[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **388062-16-6P 388062-17-7P 388062-19-9P**
388062-21-3P 388062-22-4P 388062-23-5P

388062-26-8P 388062-27-9P 388062-29-1P
388062-31-5P 388062-34-8P 388062-35-9P
388062-36-0P 388062-37-1P 388062-38-2P
388062-43-9P 388062-48-4P 388062-49-5P
388062-50-8P 388062-51-9P 388062-52-0P
388062-53-1P 388062-54-2P 388062-56-4P
388062-57-5P 388062-58-6P 388062-59-7P
388062-60-0P 388062-61-1P 388062-62-2P
388062-63-3P 388062-64-4P 388062-65-5P
388062-66-6P 388062-67-7P 388062-68-8P
388062-69-9P 388062-70-2P 388062-71-3P
388062-72-4P 388062-73-5P 388062-74-6P
388062-75-7P 388062-78-0P 388062-79-1P
388062-82-6P 388062-83-7P 388062-88-2P
388062-89-3P 388062-90-6P 388062-91-7P
388062-92-8P 388062-93-9P 388062-94-0P
388062-95-1P 388062-96-2P 388062-98-4P
388063-00-1P 388063-02-3P 388063-05-6P
388063-07-8P 388063-09-0P 388063-10-3P
388063-18-1P 388063-22-7P 388063-26-1P
388063-32-9P 388063-38-5P 388063-43-2P
388063-44-3P 388063-45-4P 388063-46-5P
388063-47-6P 388063-49-8P 388063-50-1P
388063-51-2P 388063-52-3P 388063-53-4P
388063-54-5P 388063-55-6P 388063-56-7P
388063-57-8P 388063-58-9P 388063-59-0P
388063-60-3P 388063-61-4P 388063-62-5P
388063-63-6P 388063-64-7P 388063-65-8P
388063-66-9P 388063-68-1P 388063-72-7P
388063-73-8P 388063-78-3P 388063-80-7P
388063-81-8P 388063-82-9P 388063-83-0P
388063-84-1P 388063-85-2P 388063-86-3P
388063-87-4P 388063-88-5P 388063-89-6P
388063-90-9P 388063-91-0P 388063-92-1P
388063-93-2P 388063-94-3P 388063-95-4P
388063-96-5P 388063-97-6P 388063-98-7P
388063-99-8P 388064-00-4P 388064-01-5P
388064-02-6P 388064-03-7P 388064-05-9P
388064-06-0P 388064-07-1P 388064-13-9P
388064-14-0P 388064-15-1P 388064-16-2P
388064-17-3P 388064-18-4P 388064-19-5P
388064-20-8P 388064-21-9P 388064-22-0P
388064-23-1P 388064-24-2P 388064-25-3P
388064-26-4P 388064-27-5P 388064-28-6P
388064-29-7P 388064-30-0P 388064-31-1P
388064-32-2P 388064-33-3P 388064-34-4P
388064-35-5P 388064-36-6P 388064-37-7P
388064-38-8P 388064-39-9P 388064-40-2P
388064-41-3P 388064-42-4P 388064-43-5P
388064-44-6P 388064-46-8P 388064-47-9P
388064-48-0P 388064-49-1P 388064-50-4P
388064-51-5P 388064-53-7P 388064-55-9P
388064-56-0P 388064-57-1P 388064-58-2P
388064-59-3P 388064-60-6P 388064-61-7P
388064-62-8P 388064-65-1P 388064-66-2P
388064-67-3P 388064-70-8P 388064-71-9P
388064-72-0P 388064-73-1P 388064-96-8P
388064-97-9P 388064-98-0P 388064-99-1P
388065-00-7P 388065-01-8P 388065-04-1P
388065-05-2P 388065-06-3P 388065-07-4P

09/895,871

388065-08-5P 388065-09-6P 388065-13-2P
388065-14-3P 388065-15-4P 388065-16-5P
388065-19-8P 388065-20-1P 388065-21-2P
388065-22-3P 388065-23-4P 388065-24-5P
388065-27-8P 388065-29-0P 388065-30-3P
388065-31-4P 388065-33-6P 388065-36-9P
388065-37-0P 388065-39-2P 388065-42-7P
388065-43-8P 388065-44-9P 388065-47-2P
388065-48-3P 388065-49-4P 388065-50-7P
388065-51-8P 388065-52-9P 388065-54-1P
388065-59-6P 388065-60-9P 388065-62-1P
388065-63-2P 388065-64-3P 388065-65-4P
388065-66-5P 388065-67-6P 388065-68-7P
388065-70-1P 388065-72-3P 388065-73-4P
388065-74-5P 388065-75-6P 388065-78-9P
388065-79-0P 388065-80-3P 388065-81-4P
388065-82-5P

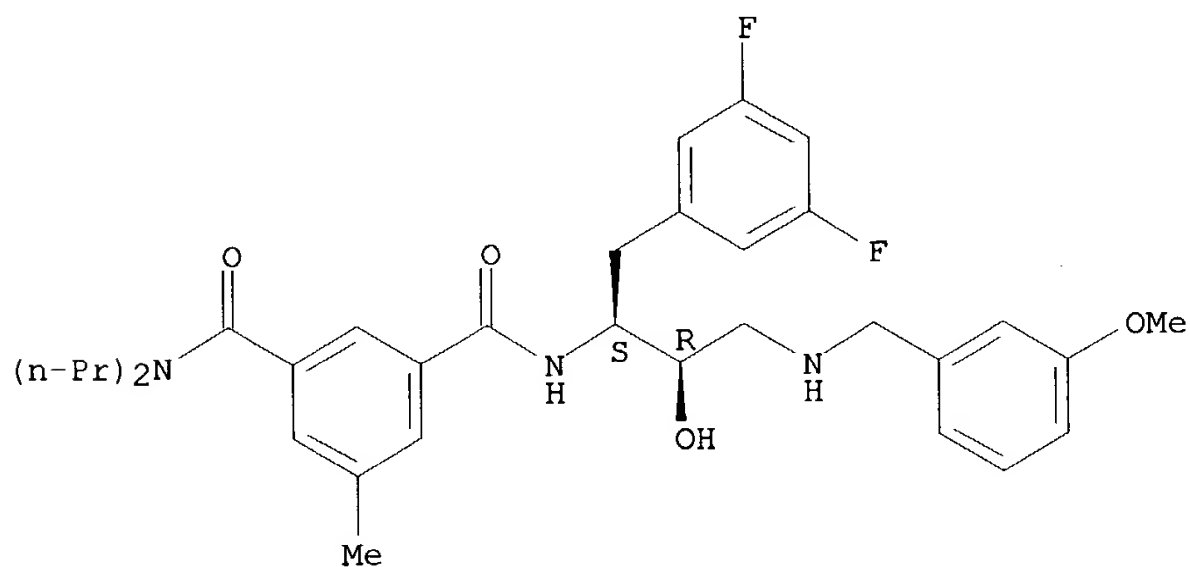
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of substituted amines for treating Alzheimer's disease)

RN 388062-16-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

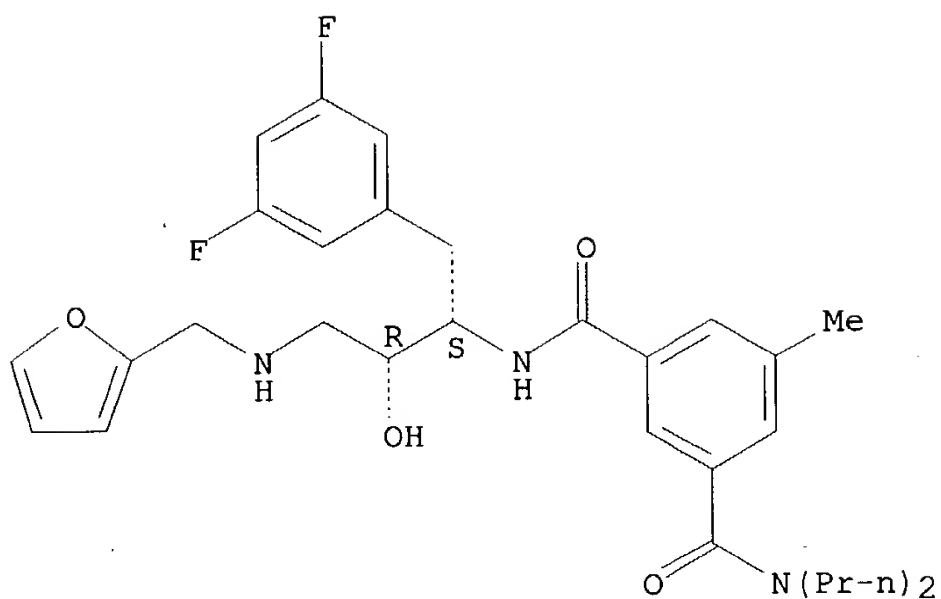


RN 388062-17-7 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[(2-furanylmethyl)amino]-2-hydroxypropyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

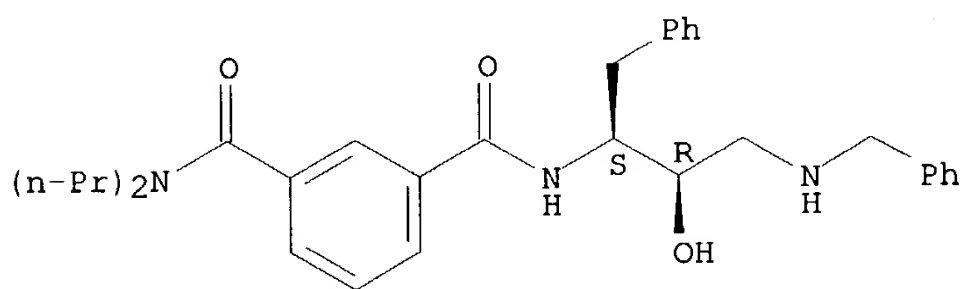
09/895,871



RN 388062-19-9 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[(phenylmethyl)amino]propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

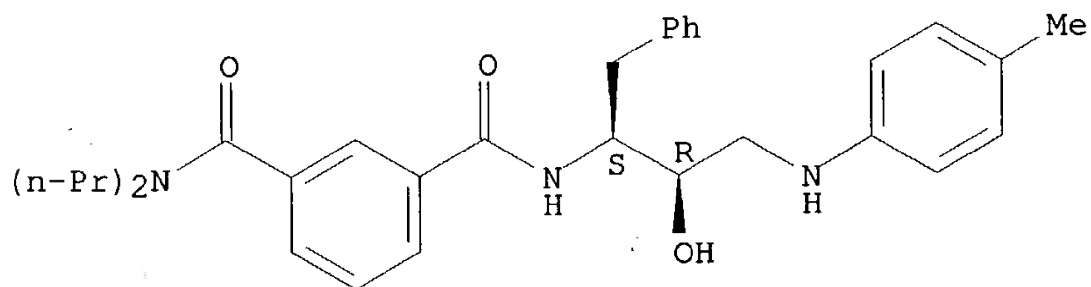
Absolute stereochemistry.



RN 388062-21-3 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[(4-methylphenyl)amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

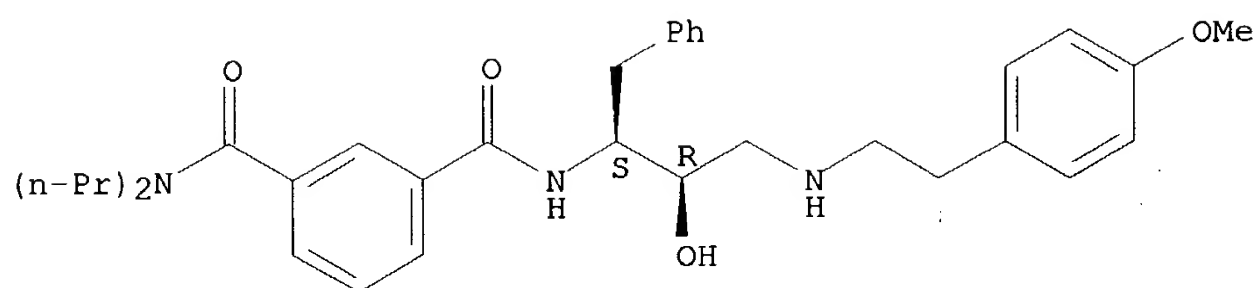


RN 388062-22-4 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[2-(4-methoxyphenyl)ethyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

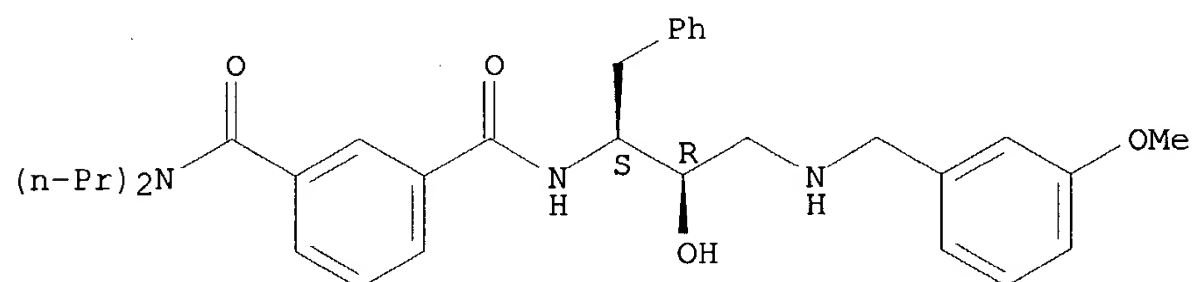
09/895,871



RN 388062-23-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI)
(CA INDEX NAME)

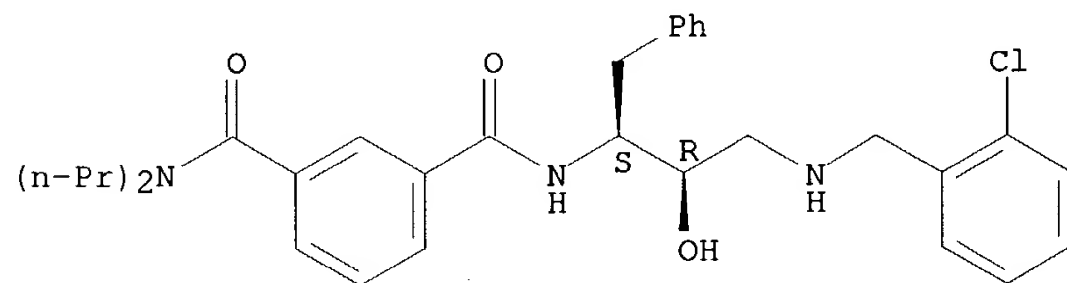
Absolute stereochemistry.



RN 388062-26-8 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-[[[2-chlorophenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

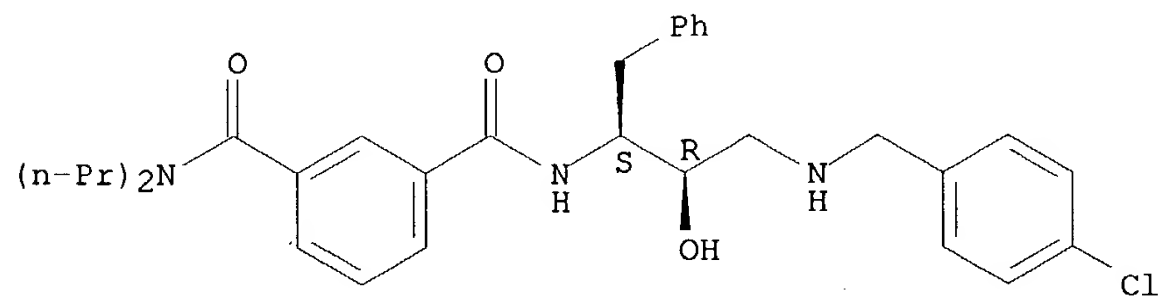
Absolute stereochemistry.



RN 388062-27-9 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-[[[4-chlorophenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

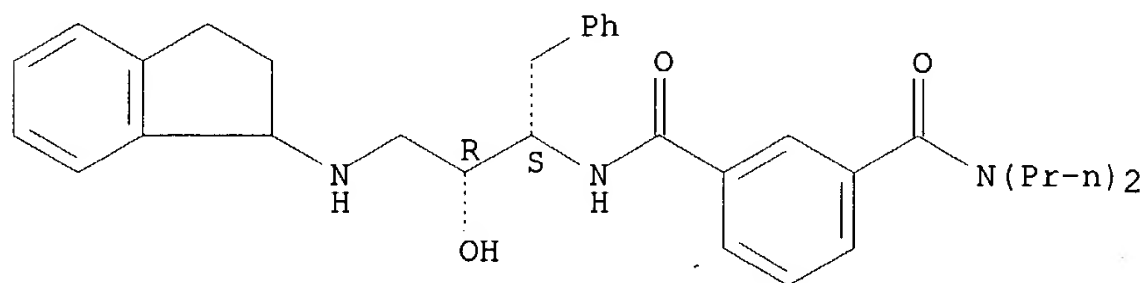


RN 388062-29-1 CAPLUS

09/895,871

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-[(2,3-dihydro-1H-inden-1-yl)amino]-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

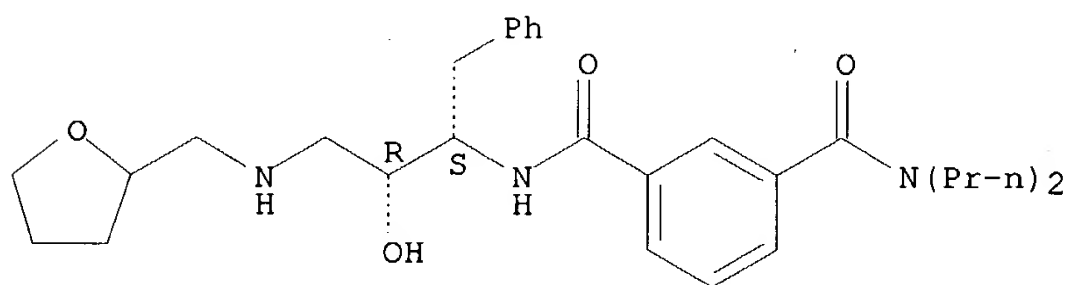
Absolute stereochemistry.



RN 388062-31-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[(tetrahydro-2-furanyl)methyl]amino]propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

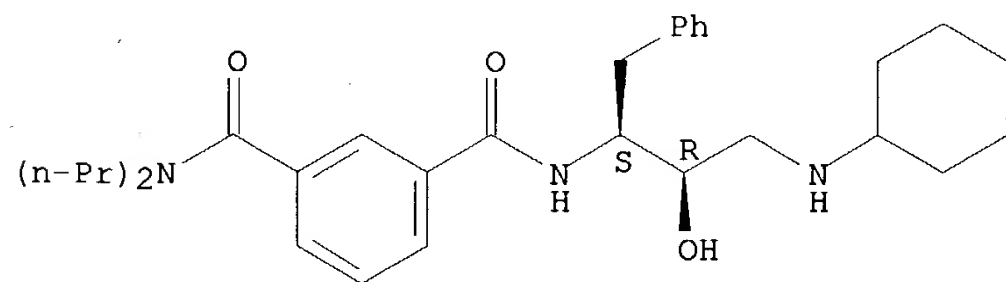
Absolute stereochemistry.



RN 388062-34-8 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-(cyclohexylamino)-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

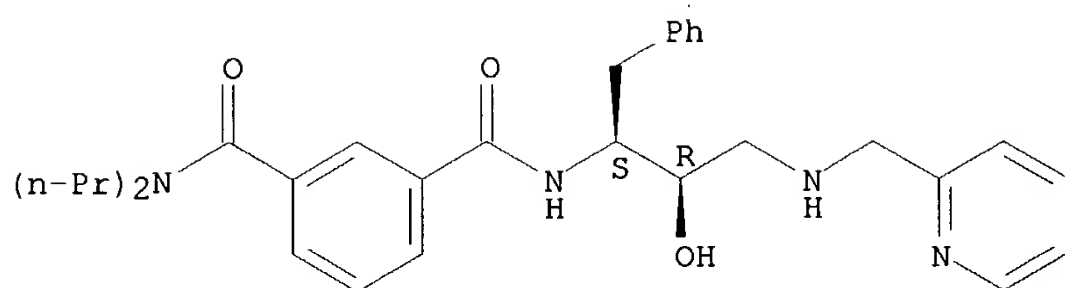


RN 388062-35-9 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[(2-pyridinylmethyl)amino]propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

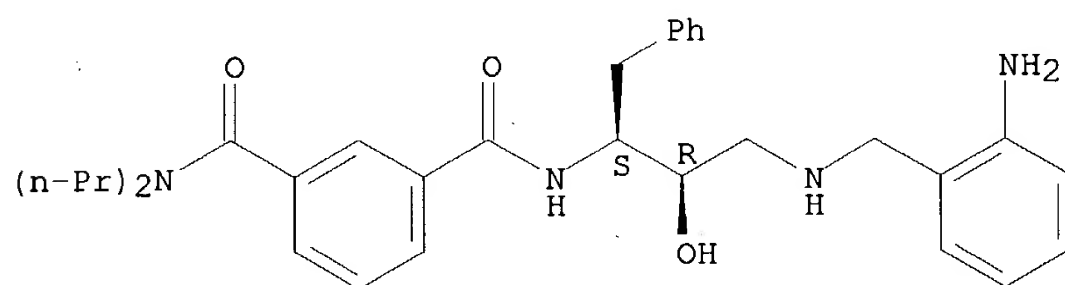
09/895,871



RN 388062-36-0 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-[[2-(aminophenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

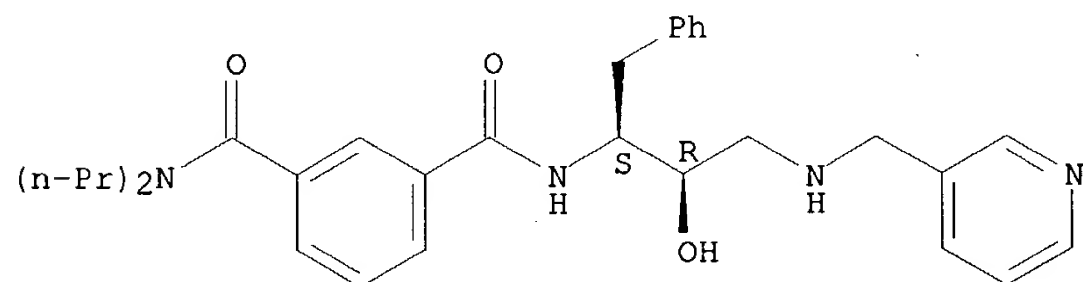
Absolute stereochemistry.



RN 388062-37-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[(3-pyridinylmethyl)amino]propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

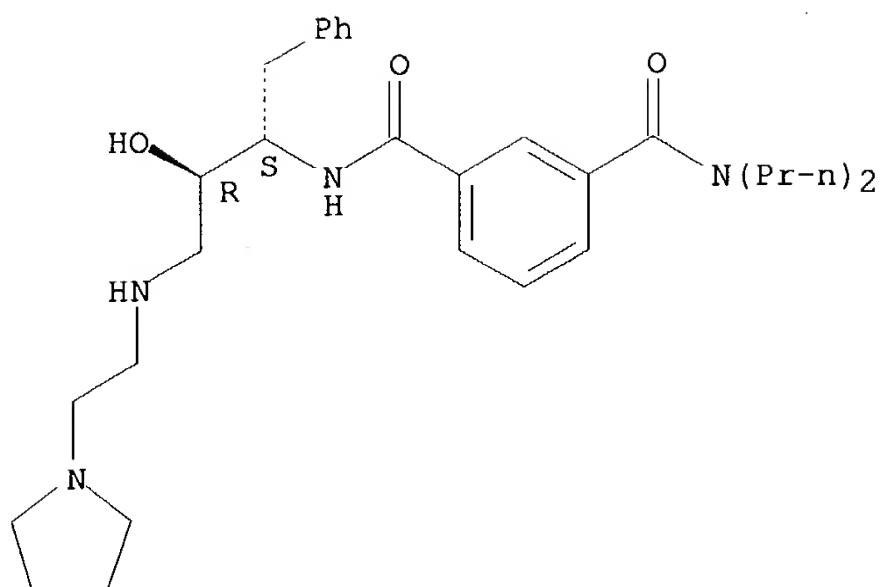


RN 388062-38-2 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[2-(1-pyrrolidinyl)ethyl]amino]propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

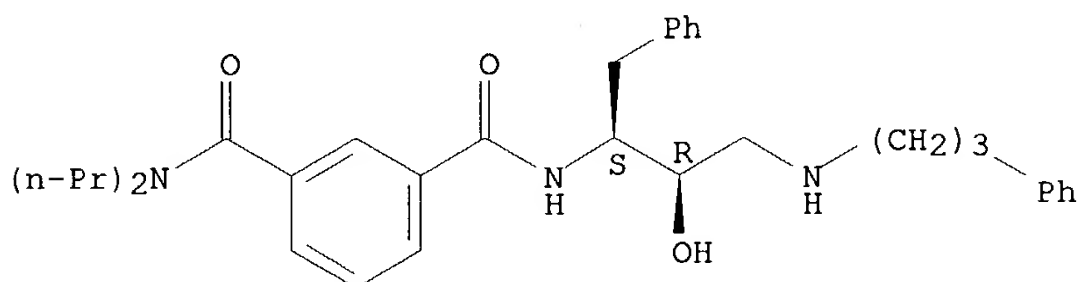
09/895,871



RN 388062-43-9 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[(3-phenylpropyl)amino]propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

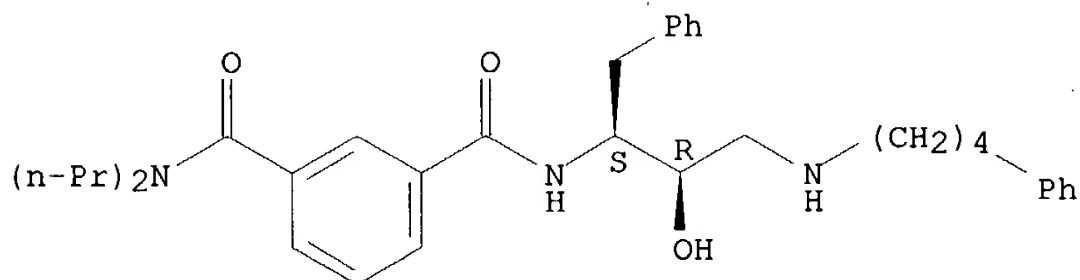
Absolute stereochemistry.



RN 388062-48-4 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[(4-phenylbutyl)amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

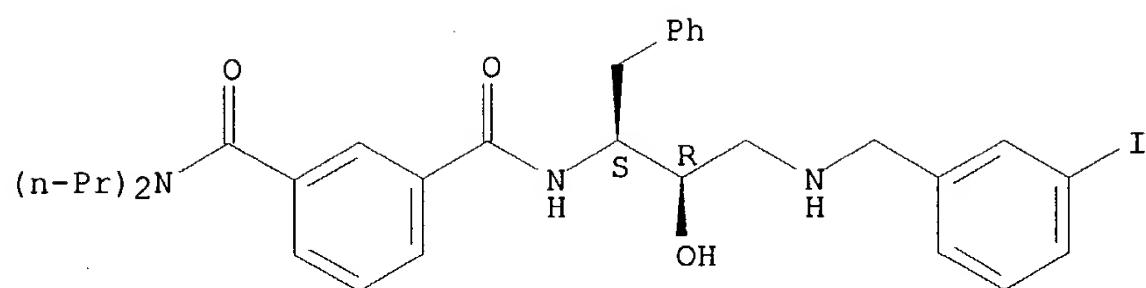


RN 388062-49-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[(3-iodophenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

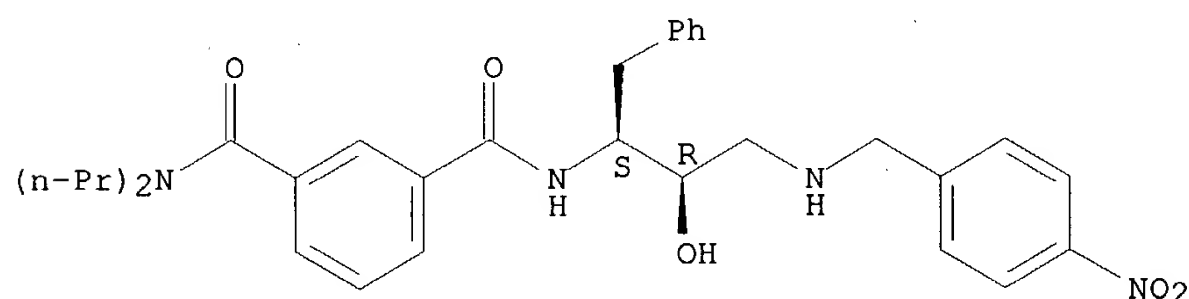
09/895,871



RN 388062-50-8 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[4-nitrophenyl]methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

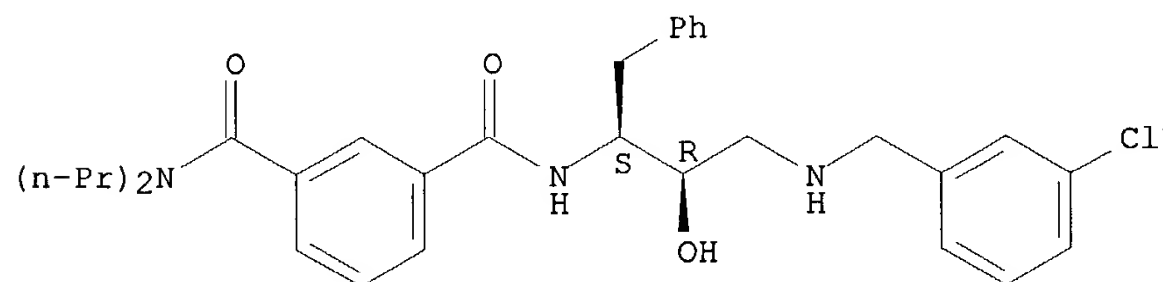
Absolute stereochemistry.



RN 388062-51-9 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-[[3-chlorophenyl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

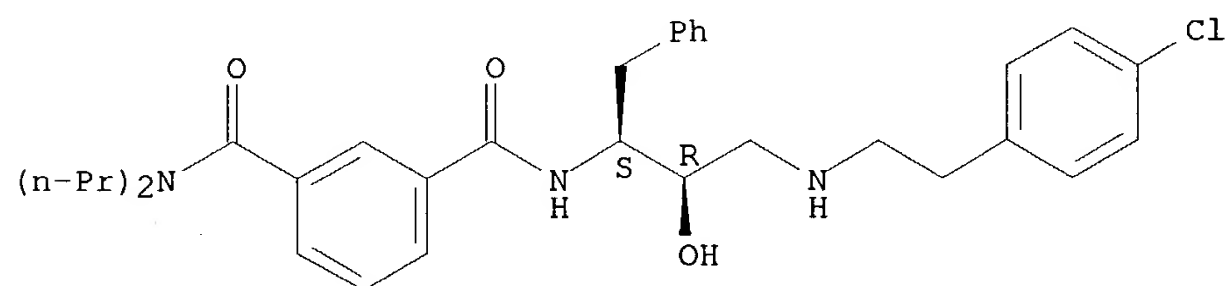
Absolute stereochemistry.



RN 388062-52-0 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-[[2-(4-chlorophenyl)ethyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

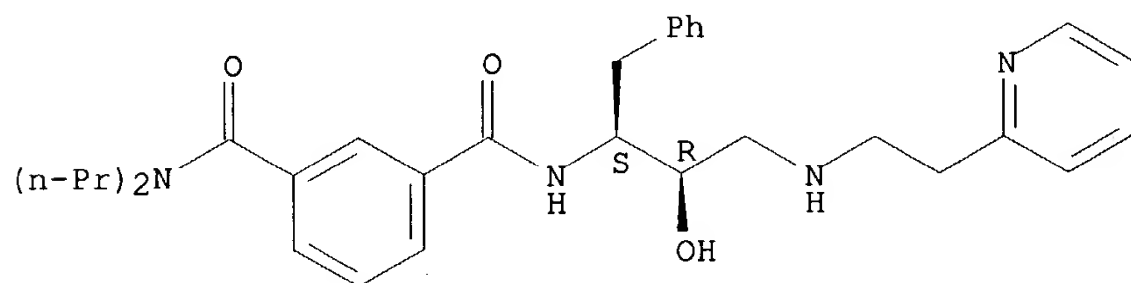


RN 388062-53-1 CAPLUS

09/895,871

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[2-(2-pyridinyl)ethyl]amino]propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

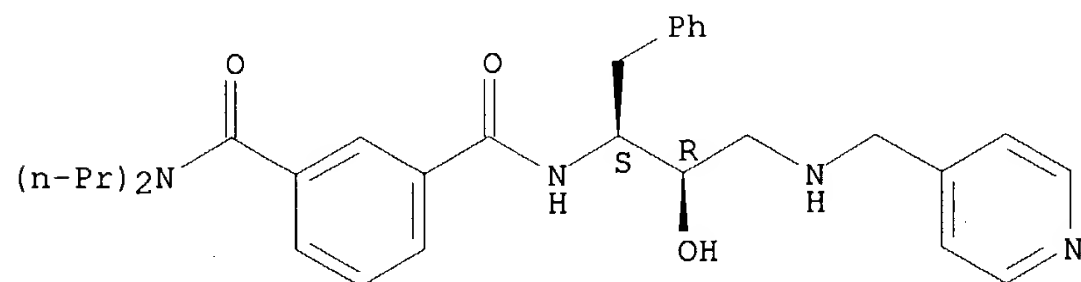
Absolute stereochemistry.



RN 388062-54-2 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[(4-pyridinylmethyl)amino]propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

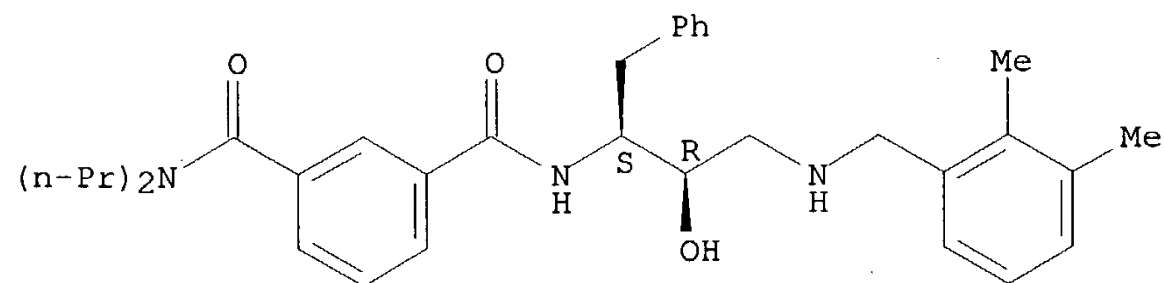
Absolute stereochemistry.



RN 388062-56-4 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-[[[2,3-dimethylphenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 388062-57-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[[2-(trifluoromethoxy)phenyl)methyl]amino]propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

09/895,871

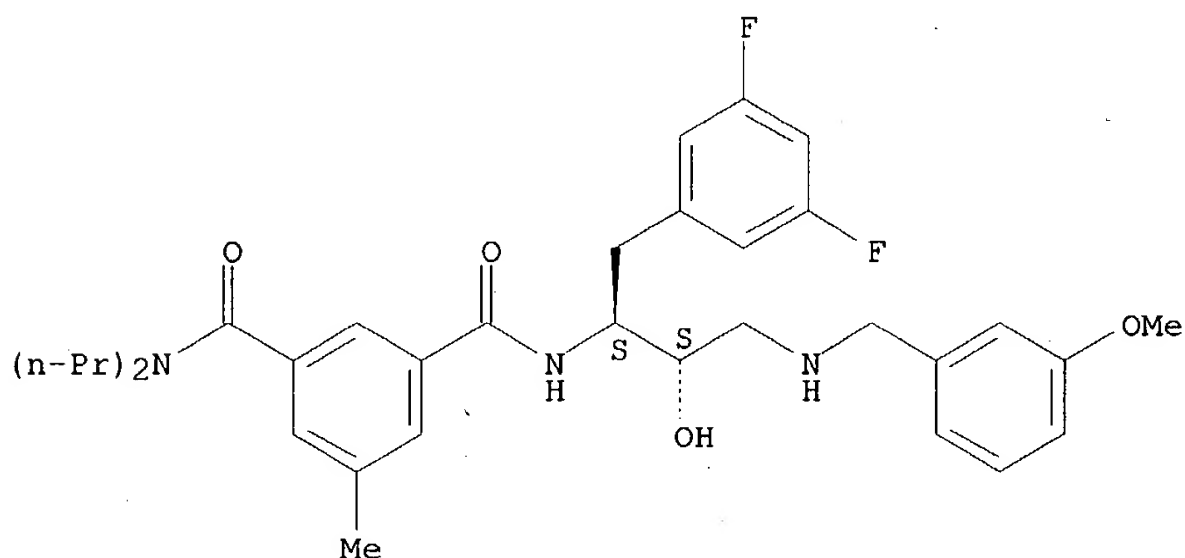
(Uses)

(preparation of substituted amines for treating Alzheimer's disease)

RN 388077-90-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2S)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[(3-methoxyphenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

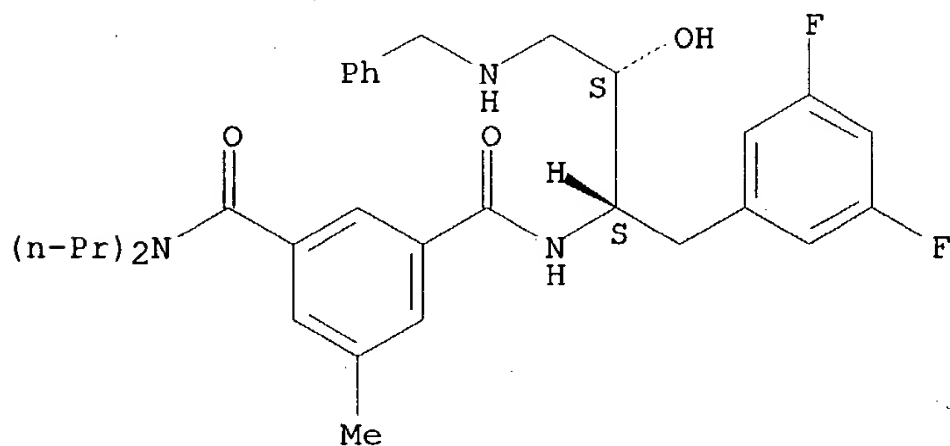
Absolute stereochemistry.



RN 388077-92-7 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2S)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[(phenylmethyl)amino]propyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:506087 CAPLUS

DOCUMENT NUMBER: 125:168656

TITLE: HIV protease inhibitors

INVENTOR(S): Abbenante, John; Bergman, Doug; Brinkworth, Ross; Dancer, Robert; Garnham, Bronwyn; Hunt, Peter; Fairlie, David; March, Darren; Martin, Jennifer; Reid, Robert

PATENT ASSIGNEE(S): University of Queensland, Australia

SOURCE: PCT Int. Appl., 84 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

09/895,871

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9616950	A1	19960606	WO 1995-AU817	19951204
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9641118	A1	19960619	AU 1996-41118	19951204
US 6043357	A	20000328	US 1997-849599	19970909
PRIORITY APPLN. INFO.:			AU 1994-9825	A 19941202
			WO 1995-AU817	W 19951204
OTHER SOURCE(S):		MARPAT 125:168656		
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

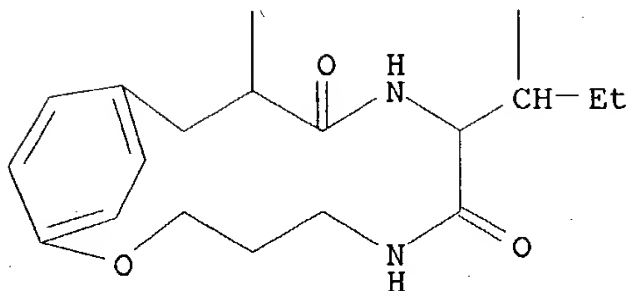
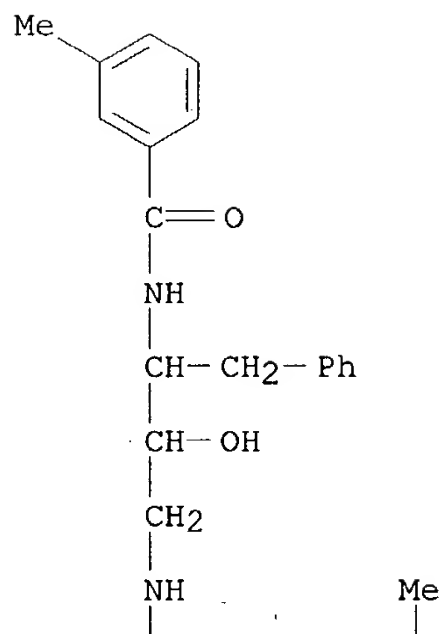
AB HIV-1 protease inhibitors which include an N-terminal ring I or a C-terminal ring II or both rings I and II [R = Asn, Ile, Val, or Glu side chain, C1-C6 alkyl, cycloalkyl; X = (CH₂)_n (n = 3-6), CH(OH)CH(OH)CH₂, CH(CO₂H)CH₂CH₂, CH₂CONHCHR₁, where R₁ = D- or L-amino acid, C1-C6 alkyl] were prepared Thus, cyclic peptide III (R and S isomers) was prepared via O-alkylation of Boc-Tyr-OH, conversion to the tyrosylmethyl bromide derivative, coupling with resin-bound H-Pro-Ile-Val-NH₂, etc. HIV-1 protease inhibitory data 134 are tabulated for 134 synthesized cyclic peptides.

IT 175170-13-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of cyclic peptides as HIV protease inhibitors)

RN 175170-13-5 CAPLUS

CN Benzamide, N-[2-hydroxy-3-[[8-(1-methylpropyl)-7,10-dioxo-2-oxa-6,9-diazabicyclo[11.2.2]heptadeca-13,15,16-trien-11-yl]amino]-1-(phenylmethyl)propyl]-3-methyl- (9CI) (CA INDEX NAME)



L5 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:172301 CAPLUS

DOCUMENT NUMBER: 124:249757

TITLE: Substrate-based cyclic peptidomimetics of Phe-Ile-Val that inhibit HIV-1 protease using a novel enzyme-binding mode

AUTHOR(S): March, Darren R.; Abbenante, Giovanni; Bergman, Douglas A.; Brinkworth, Ross I.; Wickramasinghe, Wasantha; Begun, Jake; Martin, Jennifer L.; Fairlie, David P.

CORPORATE SOURCE: Centre for Drug Design and Development, University of Queensland, Brisbane, 4072, Australia

SOURCE: Journal of the American Chemical Society (1996), 118(14), 3375-9

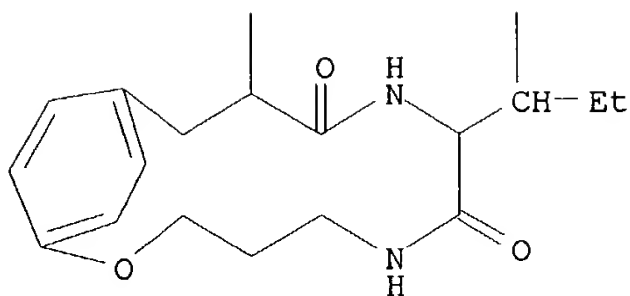
CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Results are presented for inhibitors of HIV-1 protease that demonstrate a



L5 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1985:471331 CAPLUS

DOCUMENT NUMBER: 103:71331

TITLE: Acylamino oxo or hydroxy-substituted alkylamino thiazines and thiazepines

INVENTOR(S): Weller, Harold N., III; Gordon, Eric M.; Karanewsky, Donald S.; Ryono, Denis E.

PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA

SOURCE: U.S., 16 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

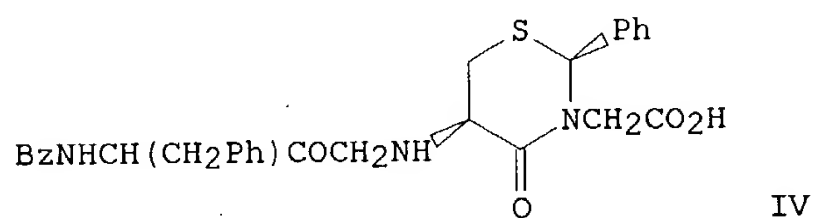
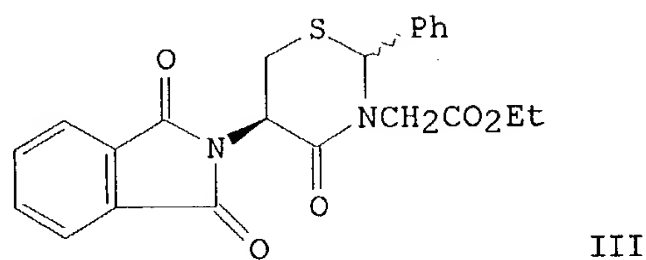
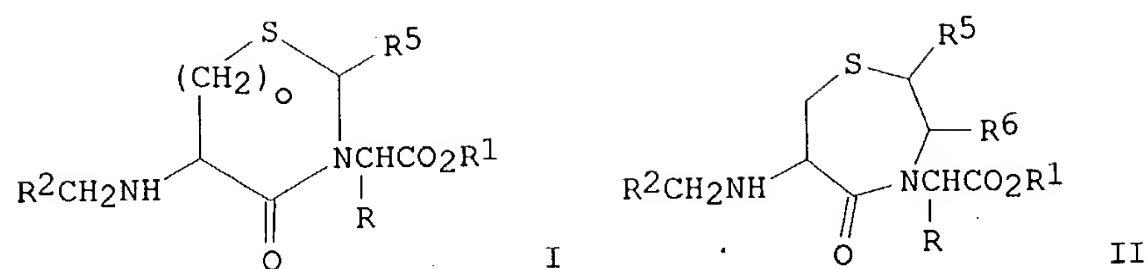
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4512988	A	19850423	US 1984-585058	19840301
AU 8539255	A1	19850912	AU 1985-39255	19850228
AU 577831	B2	19881006		
EP 154904	A1	19850918	EP 1985-102280	19850228
EP 154904	B1	19871028		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
ZA 8501555	A	19851030	ZA 1985-1555	19850228
AT 30429	E	19871115	AT 1985-102280	19850228
CA 1242438	A1	19880927	CA 1985-475365	19850228
JP 60202870	A2	19851014	JP 1985-41770	19850301
JP 06088989	B4	19941109		

PRIORITY APPLN. INFO.: US 1984-585058 A 19840301
EP 1985-102280 A 19850228

OTHER SOURCE(S): CASREACT 103:71331

GI



AB Antihypertensive (no data) thiazines and thiazepines I and II [R = H, alkyl, aminoalkyl, hydroxyalkyl, haloalkyl; R1 = H, alkyl, PhCH2, Ph2CH, Me3SiCH2CH2, salt forming ion, CHR7O2CR8 (R7 = H, alkyl, cycloalkyl, Ph; R8 = R7, alkoxy, PhCH2, PhCH2CH2); R2 = R3(CH2)mCONHCH[(CH2)nR4]C(Z); R3 = (substituted) Ph, thienyl, furyl, pyridyl; R4 = R3, OH, NH2, SH, halo, indolyl, imidazolyl, alkylthio, guanidino, carbamoyl, cycloalkyl; m = 0-4; n = 1-4; Z = O, (H, OH); R5, R6 = H, alkyl, cycloalkylalkyl, R5R6 = benzo; o = 1, 2] were prepared via inter- and intramol. cyclocondensations of cysteine derivs. Thus, cyclocondensation of N-phthaloyl-L-cysteine with PhCH:NCH2CO2Et gave thiazineacetate III as a mixture of diastereomers, the (2S)-isomer of which was transesterified with Me3SiCH2CH2OH, deprotected, alkylated with (S)-PhCH2CH(NHBz)COCH2Cl and hydrolyzed to give [2S-[2α,5α(S)]]-thiazine IV.

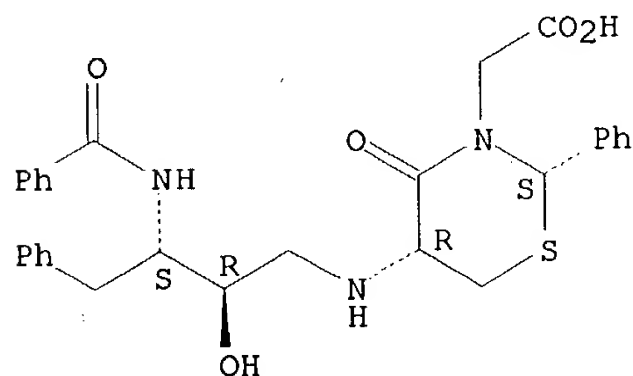
IT 97246-59-8P 97549-62-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 97246-59-8 CAPLUS

2H-1,3-Thiazine-3(4H)-acetic acid, 5-[[3-(benzoylamino)-2-hydroxy-4-phenylbutyl]amino]dihydro-4-oxo-2-phenyl-, [2S-[2 α ,5 α (2S*,3R*)]]- (9CI) (CA INDEX NAME)

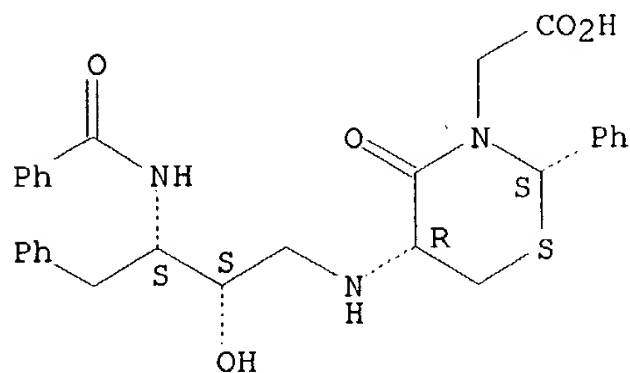
Absolute stereochemistry.



09/895,871

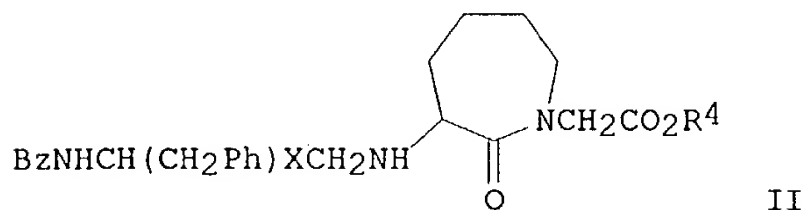
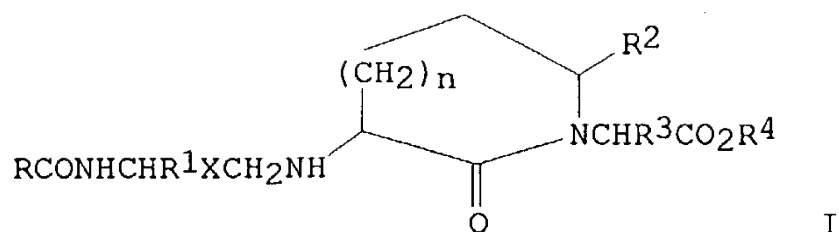
RN 97549-62-7 CAPLUS
CN 2H-1,3-Thiazine-3(4H)-acetic acid, 5-[[3-(benzoylamino)-2-hydroxy-4-phenylbutyl]amino]dihydro-4-oxo-2-phenyl-, [2S-[2 α ,5 α (2R*,3R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1985:78746 CAPLUS
DOCUMENT NUMBER: 102:78746
TITLE: Lactam-containing compounds, their pharmaceutical compositions and use
INVENTOR(S): Gordon, Eric M.; Karanewsky, Donald S.
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: U.S., 13 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4474778	A	19841002	US 1983-549931	19831109
AU 8435220	A1	19850516	AU 1984-35220	19841108
EP 142335	A2	19850522	EP 1984-307723	19841108
EP 142335	A3	19870513		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
ZA 8408743	A	19850731	ZA 1984-8743	19841108
JP 60115565	A2	19850622	JP 1984-236582	19841109
PRIORITY APPLN. INFO.:			US 1983-549931	A 19831109
OTHER SOURCE(S):	CASREACT 102:78746			
GI				



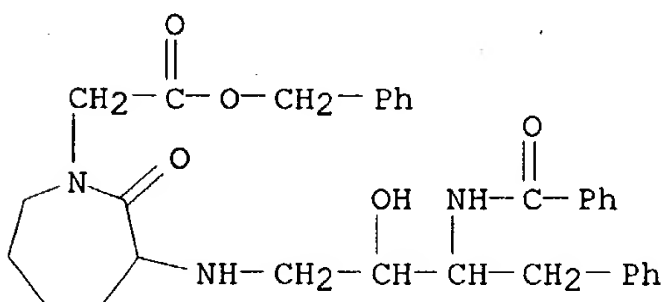
AB Antihypertensive (no data) lactams I [$n = 1-4$; $X = \text{CO}, \text{CHOH}$; $R = R_5$; $R_1 = \text{H}, \text{alkyl}, R_5, \text{cycloalkyl}, \text{cycloalkylalkyl}, 3\text{-indolyl}, 3\text{-indolylalkyl}, \text{hydroxyalkyl}, \text{imidazolylalkyl}, \text{aminoalkyl}, \text{mercaptoalkyl}, \text{alkylthioalkyl}, \text{guanidinoalkyl}, \text{carbamoylalkyl}$; $R_2 = \text{H}, \text{alkyl}, \text{cycloalkyl}, \text{cycloalkylalkyl}, R_5$, $R_3 = \text{H}, \text{alkyl}, \text{aminoalkyl}, \text{hydroxyalkyl}, \text{haloalkyl}$; $R_4 = \text{H}, \text{alkyl}, \text{CH}_2\text{Ph}, \text{CHPh}_2, 1\text{-acyloxyalkyl}, \text{cation}$; $R_5 = (\text{un})\text{substituted Ph}, \text{phenylalkyl}, \text{thienyl}, \text{thienylalkyl}, \text{furyl}, \text{furylalkyl}, \text{pyridyl}, \text{pyridylalkyl}$] were prepared. Thus, (S)-II ($R_4 = \text{H}, X = \text{CO}$) was prepared from $\text{Me}_3\text{CO}_2\text{C-Lys}(\text{CO}_2\text{CH}_2\text{Ph})\text{-OH}$ and (S)- $\text{BzNHCH}(\text{CH}_2\text{Ph})\text{COCH}_2\text{Cl}$ in 6 steps. II ($R_4 = \text{CH}_2\text{Ph}, X = \text{CO}$) was reduced with NaBH_4 and hydrogenolyzed over Pd-C to give II ($R_4 = \text{H}, X = \text{CHOH}$).

IT **93960-65-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of)

RN 93960-65-7 CAPLUS

CN 1H-Azepine-1-acetic acid, 3-[[3-(benzoylamino)-2-hydroxy-4-phenylbutyl]amino]hexahydro-2-oxo-, phenylmethyl ester (9CI) (CA INDEX NAME)



IT **93960-66-8P 93960-67-9P 93960-71-5P**

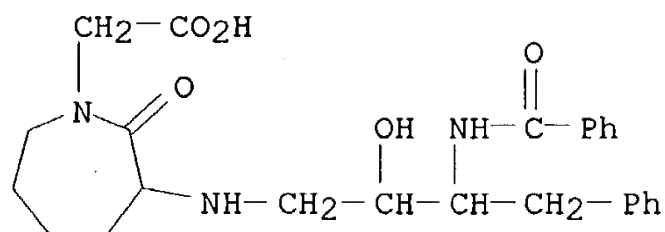
93960-72-6P 93960-73-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 93960-66-8 CAPLUS

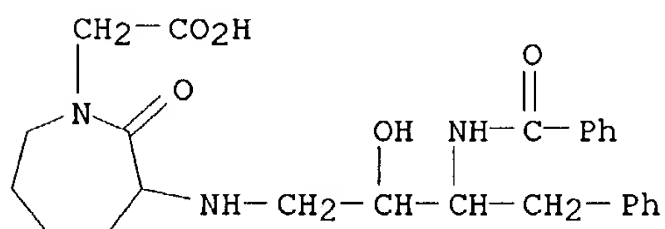
CN 1H-Azepine-1-acetic acid, 3-[[3-(benzoylamino)-2-hydroxy-4-phenylbutyl]amino]hexahydro-2-oxo- (9CI) (CA INDEX NAME)

09/895,871



RN 93960-67-9 CAPLUS

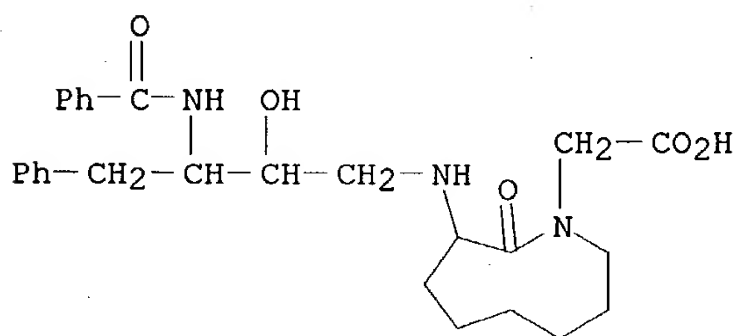
CN 1H-Azepine-1-acetic acid, 3-[[3-(benzoylamino)-2-hydroxy-4-phenylbutyl]amino]hexahydro-2-oxo-, monosodium salt (9CI) (CA INDEX NAME)



● Na

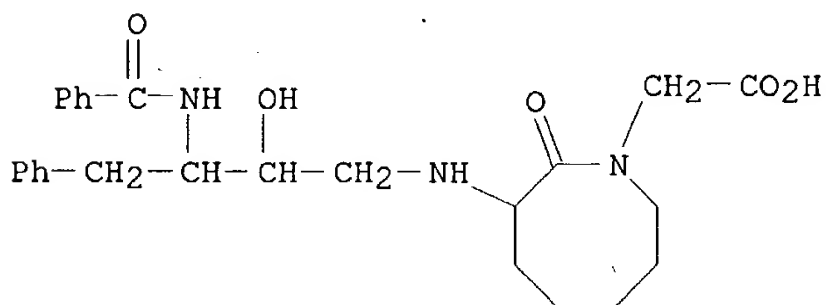
RN 93960-71-5 CAPLUS

CN 1H-Azonine-1-acetic acid, 3-[[3-(benzoylamino)-2-hydroxy-4-phenylbutyl]amino]octahydro-2-oxo- (9CI) (CA INDEX NAME)



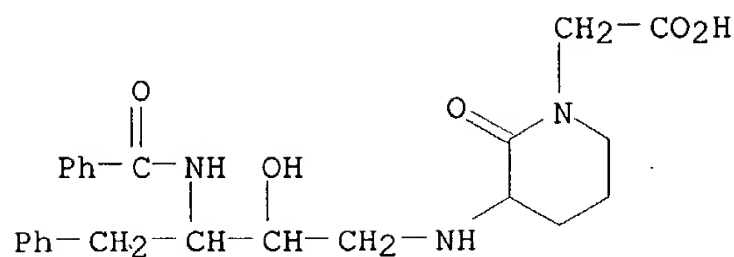
RN 93960-72-6 CAPLUS

CN 1(2H)-Azocineacetic acid, 3-[[3-(benzoylamino)-2-hydroxy-4-phenylbutyl]amino]hexahydro-2-oxo- (9CI) (CA INDEX NAME)



RN 93960-73-7 CAPLUS

CN 1-Piperidineacetic acid, 3-[[3-(benzoylamino)-2-hydroxy-4-phenylbutyl]amino]-2-oxo- (9CI) (CA INDEX NAME)



=> d 16 1-7 ibib abs hitstr

L6 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:956793 CAPLUS

TITLE: Structure-Based Design of Potent and Selective Cell-Permeable Inhibitors of Human β -Secretase (BACE-1)

AUTHOR(S): Stachel, Shawn J.; Coburn, Craig A.; Steele, Thomas G.; Jones, Kristen G.; Loutzenhiser, Elizabeth F.; Gregro, Alison R.; Rajapakse, Hemaka A.; Lai, Ming-Tain; Crouthamel, Ming-Chih; Xu, Min; Tugusheva, Katherine; Lineberger, Janet E.; Pietrak, Beth L.; Espeseth, Amy S.; Shi, Xiao-Ping; Chen-Dodson, Elizabeth; Holloway, M. Katharine; Munshi, Sanjeev; Simon, Adam J.; Kuo, Lawrence; Vacca, Joseph P.

CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, West Point, PA, 19486, USA

SOURCE: Journal of Medicinal Chemistry (2004), 47(26), 6447-6450

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We describe the development of cell-permeable β -secretase inhibitors that demonstratively inhibit the production of the secreted amino terminal fragment of an artificial amyloid precursor protein in cell culture. In addition to potent inhibition in a cell-based assay ($IC_{50} < 100$ nM), these inhibitors display impressive selectivity against other biol. relevant aspartyl proteases.

IT 797035-16-6P

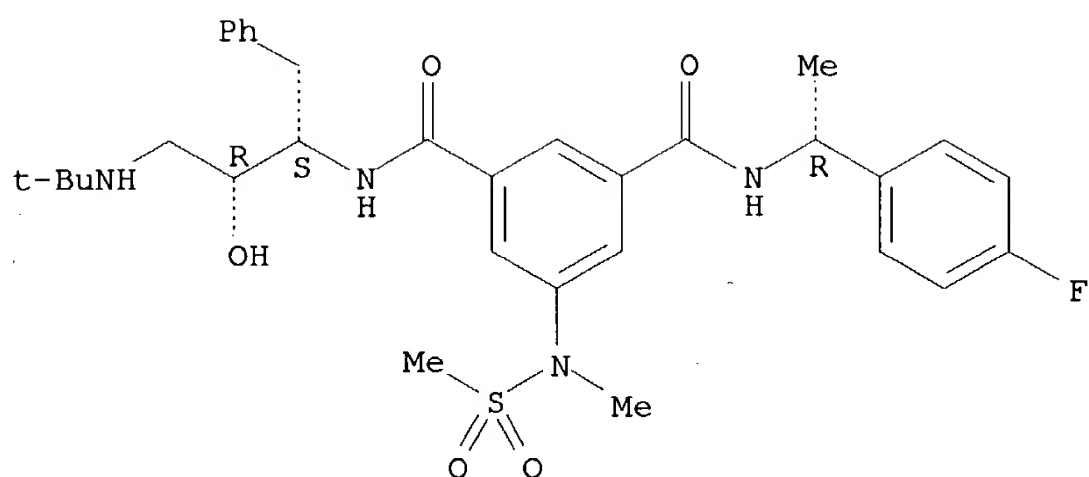
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(structure-based design of potent and selective cell-permeable inhibitors of human β -secretase (BACE-1))

RN 797035-16-6 CAPLUS

CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:927212 CAPLUS

DOCUMENT NUMBER: 141:395588

TITLE: Preparation of hydroxydiaminopropyl tricyclic indolecarboxamides for treatment of β -amyloid related disease.

INVENTOR(S): Demont, Emmanuel Hubert; Redshaw, Sally; Walter, Daryl Simon

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 74 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094430	A1	20041104	WO 2004-EP4244	20040421
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:

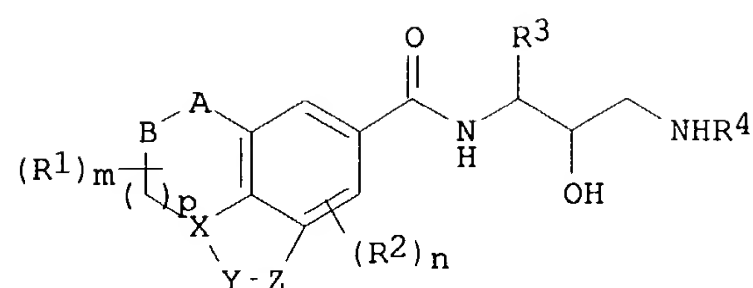
GB 2003-9221

A 20030423

OTHER SOURCE(S):

MARPAT 141:395588

GI



I

AB Title compds. [I; R1, R2 = alkyl, alkenyl, halo, alkoxy, amino, cyano, OH; m, n = 0-2; p = 1, 2; AB = NR5SO2, NR5CO; R5 = H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, aralkyl, heteroaralkyl, arylcycloalkyl, heteroarylalkyl; XYZ = NCR8:CR9; R8 = H, alkyl, cycloalkyl; R9 = R8, aryl, heteroaryl, aralkyl, heteroarylalkyl, etc.; R3 = (substituted) alkyl, alkenyl, alkynyl, alkylcycloalkyl, alkylaryl, alkylheteroaryl, alkylheterocyclyl; R4 = H, (substituted) alkyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, alkylcycloalkyl, cycloalkylaryl, heterocyclylaryl, etc.], were prepared Thus, 7-ethyl-2-oxo-1,2,3,4-tetrahydro[1,4]diazepino[3,2,1-hi]indole-9-carboxylic acid (preparation given), (2R,3S)-3-amino-1-(3-methoxybenzylamino)-4-phenylbutan-2-ol ditosylate, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, 1-hydroxybenzotriazole hydrate, and 4-ethylmorpholine were stirred 4 h in CH2Cl2/DMF to give 7-ethyl-2-oxo-1,2,3,4-tetrahydro[1,4]diazepino[3,2,1-hi]indole-9-carboxylic acid [(1S,2R)-1-benzyl-2-hydroxy-3-(3-methoxybenzylamino)propyl]amide. I inhibited Asp-2 with IC50 <10 μ M.

IT 790252-30-1P 790252-40-3P 790252-79-8P
790253-08-6P 790253-11-1P 790253-17-7P
790253-19-9P 790253-21-3P 790253-76-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of hydroxydiaminopropyl tricyclic indolecarboxamides for treatment of β -amyloid related disease)

RN 790252-30-1 CAPLUS

CN Formic acid, compd. with 7-ethyl-3,4-dihydro-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-1-methyl-1H-pyrrolo[1,2,3-ef]-2,1,5-benzothiadiazepine-9-carboxamide 2,2-dioxide (1:1) (9CI) (CA INDEX NAME)

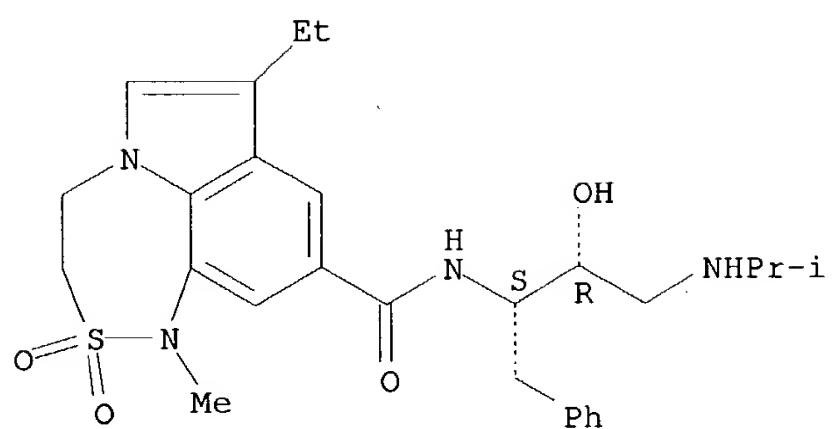
CM 1

CRN 790252-29-8

CMF C27 H36 N4 O4 S

Absolute stereochemistry.

09/895,871



CM 2

CRN 64-18-6

CMF C H2 O2

O=CH-OH

RN 790252-40-3 CAPLUS

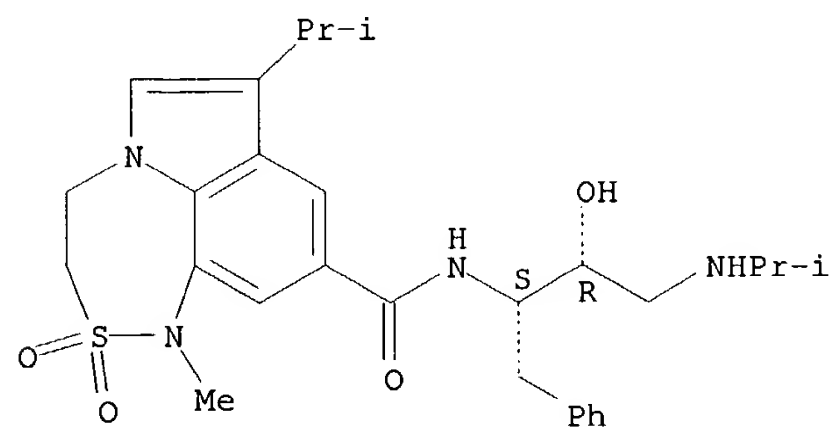
CN Formic acid, compd. with 3,4-dihydro-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-1-methyl-7-(1-methylethyl)-1H-pyrrolo[1,2,3-ef]-2,1,5-benzothiadiazepine-9-carboxamide 2,2-dioxide (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 790252-39-0

CMF C28 H38 N4 O4 S

Absolute stereochemistry.



CM 2

CRN 64-18-6

CMF C H2 O2

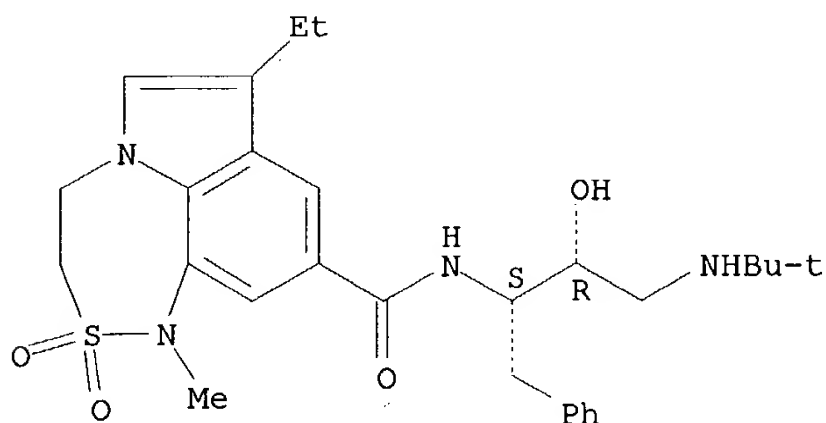
O=CH-OH

RN 790252-79-8 CAPLUS

09/895,871

CN 1H-Pyrrolo[1,2,3-ef]-2,1,5-benzothiadiazepine-9-carboxamide,
N-[(1S,2R)-3-[(1,1-dimethylethyl)amino]-2-hydroxy-1-(phenylmethyl)propyl]-
7-ethyl-3,4-dihydro-1-methyl-, 2,2-dioxide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 790253-08-6 CAPLUS

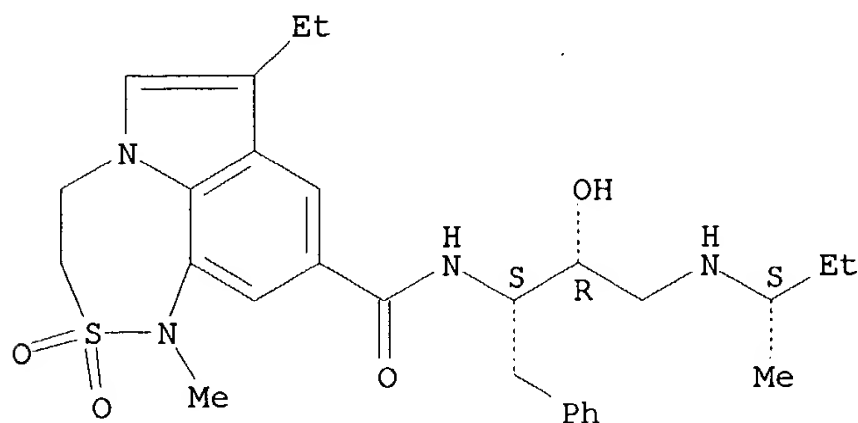
CN Formic acid, compd. with 7-ethyl-3,4-dihydro-N-[(1S,2R)-2-hydroxy-3-[[(1S)-
1-methylpropyl]amino]-1-(phenylmethyl)propyl]-1-methyl-1H-pyrrolo[1,2,3-
ef]-2,1,5-benzothiadiazepine-9-carboxamide 2,2-dioxide (1:1) (9CI) (CA
INDEX NAME)

CM 1

CRN 790253-07-5

CMF C28 H38 N4 O4 S

Absolute stereochemistry.



CM 2

CRN 64-18-6

CMF C H2 O2

O=CH-OH

RN 790253-11-1 CAPLUS

CN Formic acid, compd. with N-[(1S,2R)-3-(3-butylamino)-2-hydroxy-1-
(phenylmethyl)propyl]-7-ethyl-3,4-dihydro-1-methyl-1H-pyrrolo[1,2,3-ef]-
2,1,5-benzothiadiazepine-9-carboxamide 2,2-dioxide (1:1) (9CI) (CA INDEX
NAME)

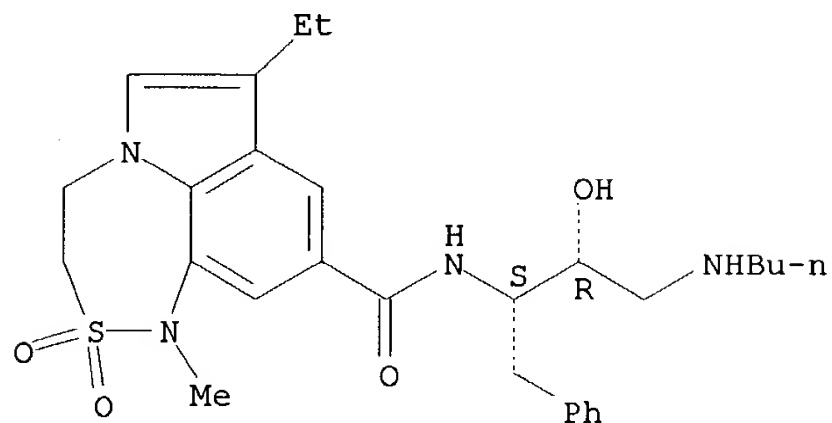
09/895,871

CM 1

CRN 790253-10-0

CMF C28 H38 N4 O4 S

Absolute stereochemistry.



CM 2

CRN 64-18-6

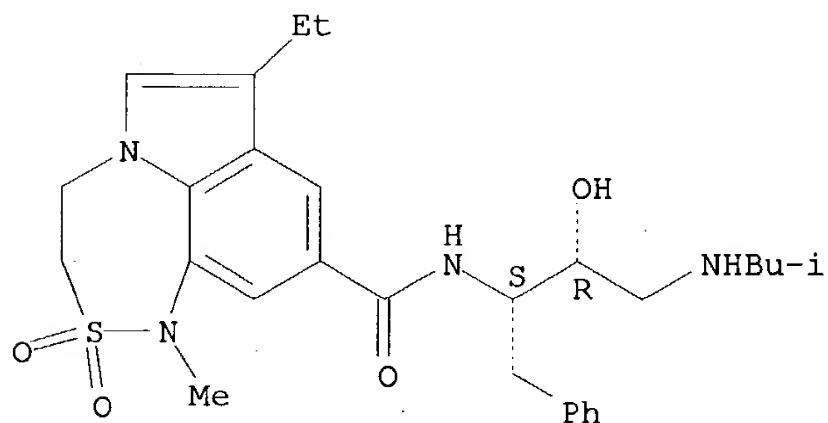
CMF C H2 O2

O=CH-OH

RN 790253-17-7 CAPLUS

CN 1H-Pyrrolo[1,2,3-ef]-2,1,5-benzothiadiazepine-9-carboxamide,
7-ethyl-3,4-dihydro-N-[(1S,2R)-2-hydroxy-3-[(2-methylpropyl)amino]-1-(phenylmethyl)propyl]-1-methyl-, 2,2-dioxide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

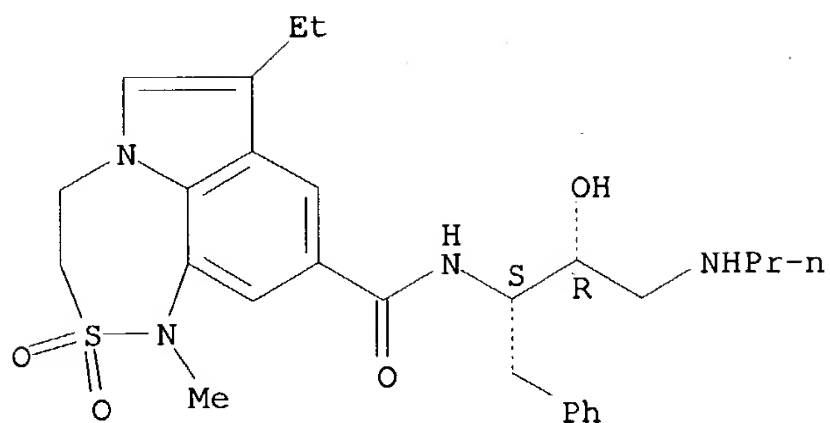


RN 790253-19-9 CAPLUS

CN 1H-Pyrrolo[1,2,3-ef]-2,1,5-benzothiadiazepine-9-carboxamide,
7-ethyl-3,4-dihydro-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-(propylamino)propyl]-1-methyl-, 2,2-dioxide (9CI) (CA INDEX NAME)

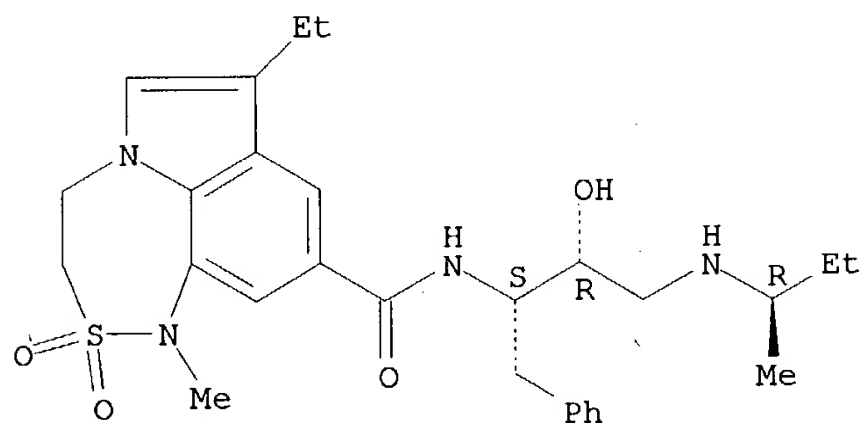
Absolute stereochemistry.

09/895,871



RN 790253-21-3 CAPLUS
CN 1H-Pyrrolo[1,2,3-ef]-2,1,5-benzothiadiazepine-9-carboxamide,
7-ethyl-3,4-dihydro-N-[(1S,2R)-2-hydroxy-3-[(1R)-1-methylpropyl]amino]-1-(phenylmethyl)propyl]-1-methyl-, 2,2-dioxide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

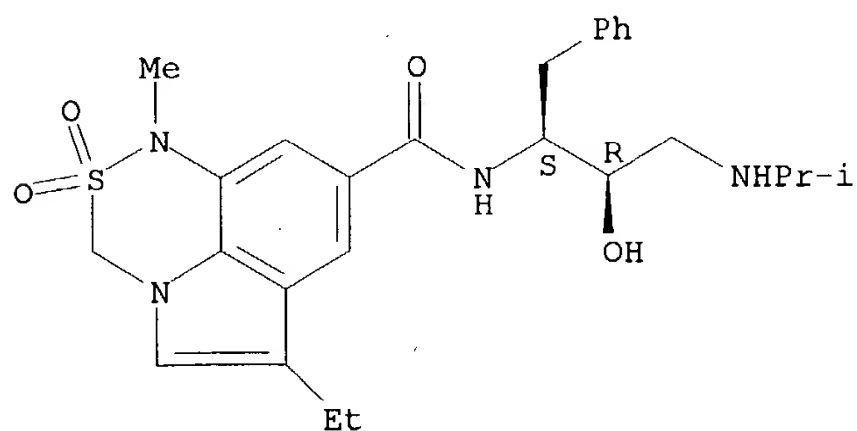


RN 790253-76-8 CAPLUS
CN Formic acid, compd. with 6-ethyl-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-1-methyl-1H,3H-pyrrolo[1,2,3-de]-2,1,4-benzothiadiazine-8-carboxamide 2,2-dioxide (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 790253-75-7
CMF C26 H34 N4 O4 S

Absolute stereochemistry.



09/895,871

CM 2

CRN 64-18-6
CMF C H2 O2

O=CH-OH

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:493673 CAPLUS

DOCUMENT NUMBER: 141:54189

TITLE: Preparation of hydroxyethylamine derivatives for the
treatment of Alzheimer's disease

INVENTOR(S): Demont, Emmanuel H.; Faller, Andrew; MacPherson, David
Timothy; Milner, Peter Henry; Naylor, Alan; Redshaw,
Sally; Stanway, Steven James; Vesey, David R.; Walter,
Daryl S.

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 201 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004050619	A1	20040617	WO 2003-EP13806	20031203
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.:

GB 2002-28410

A 20021205

OTHER SOURCE(S): MARPAT 141:54189

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = alkyl, alkenyl, halo, etc.; R2' = H, alkyl, alkoxy, halo; m, n = 0-2; X = CO, SO, SO2; p = 1-3; R2 = H, alk(en)yl, (hetero)aryl, etc.; R3 = halo, alk(en)yl, (hetero)aryl, etc.; R4 = alkynyl, alkylaryl, etc.; R5 = H, alkyl, cycloalkyl, cycloalkenyl, etc.] are prepared For instance, 5-(2-oxopyrrolidin-1-yl)-N,N-dipropylisophthalamide (preparation given) is coupled to (2S)-2-(((2R,3S)-3-amino-2-hydroxy-4-phenylbutyl)amino)-N-cyclohexylpropionamide (preparation given) (DMF, EDCI, HOBT, 4-ethylmorpholine, 3 h) to give II. Compds. of the invention inhibit protease Asp2 and Cathepsin D. I are useful in the

treatment of diseases characterized by elevated amyloid levels or amyloid deposits, particularly Alzheimer's disease.

IT **706796-41-0P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(isopropylamino)propyl]-3-ethylamino-5-(2-oxopyrrolidin-1-yl)benzamide
706796-54-5P, N-[(1S,2R)-1-Benzyl-3-tert-butylamino-2-hydroxypropyl]-3-ethylamino-5-(2-oxopyrrolidin-1-yl)benzamide
706796-69-2P, N-[1-Benzyl-2-hydroxy-3-(isobutylamino)propyl]-3-ethylamino-5-(2-oxopyrrolidin-1-yl)benzamide **706796-71-6P**, N-[1-Benzyl-2-hydroxy-3-(propylamino)propyl]-3-ethylamino-5-(2-oxopyrrolidin-1-yl)benzamide **706797-99-1P**, 4-(1,1-Dioxotetrahydro-2H-1,2-thiazin-2-yl)-1-ethyl-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-1H-benzimidazole-6-carboxamide
706798-00-7P, 8-(1,1-Dioxoisothiazolidin-2-yl)-4-ethyl-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-1,2,3,4-tetrahydro-6-quinoxalinecarboxamide **706799-04-4P**, 3-(1,1-Dioxotetrahydro-2H-1,2-thiazin-2-yl)-5-(ethylamino)-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-(propylamino)propyl]benzamide hydrochloride
706799-09-9P 706800-33-1P, N-[(1S,2R)-3-(Butylamino)-2-hydroxy-1-(phenylmethyl)propyl]-3-(1,1-dioxotetrahydro-2H-1,2-thiazin-2-yl)-5-(ethylamino)benzamide hydrochloride **706801-48-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(isopropylamino)propyl]-3-ethyl-7-(2-oxopyrrolidin-1-yl)-1H-indole-5-carboxamide formate **706801-59-4P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(isopropylamino)propyl]-7-(1,1-dioxoisothiazolidin-2-yl)-3-ethyl-1H-indole-5-carboxamide formate
706801-64-1P 706801-96-9P, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(isopropylamino)propyl]-3-(1,1-dioxo-1,2-thiazinan-2-yl)-5-(isopropylamino)benzamide formate **706802-41-7P 706802-47-3P**, 5-(Ethylamino)-2-fluoro-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-3-(2-oxo-1-pyrrolidinyl)benzamide **706802-58-6P**, 3-(1,1-Dioxotetrahydro-2H-1,2-thiazin-2-yl)-5-(ethylamino)-2-fluoro-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]benzamide **706802-75-7P**, 4-(1,1-Dioxoisothiazolidin-2-yl)-1-ethyl-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-1H-indazole-6-carboxamide
706804-22-0P 706805-16-5P

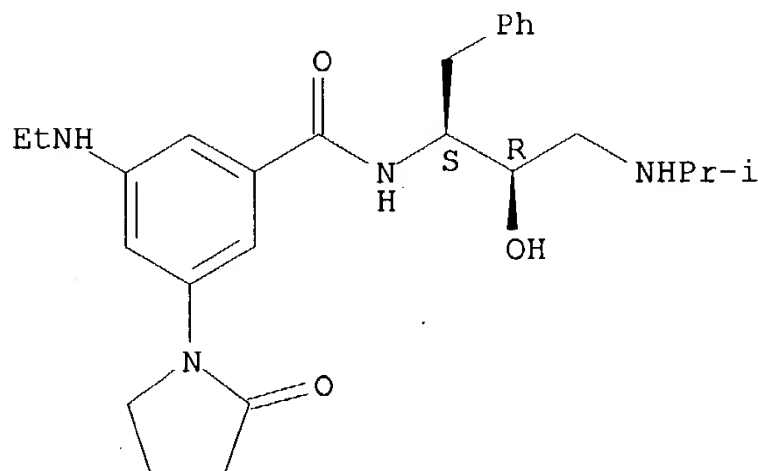
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of hydroxyethylamine derivs. for treatment of Alzheimer's disease)

RN 706796-41-0 CAPLUS

CN Benzamide, 3-(ethylamino)-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-5-(2-oxo-1-pyrrolidinyl)- (9CI) (CA INDEX NAME)

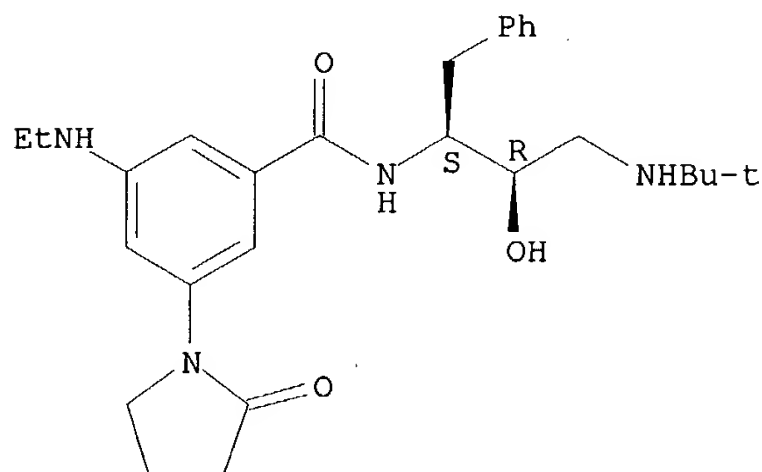
Absolute stereochemistry.



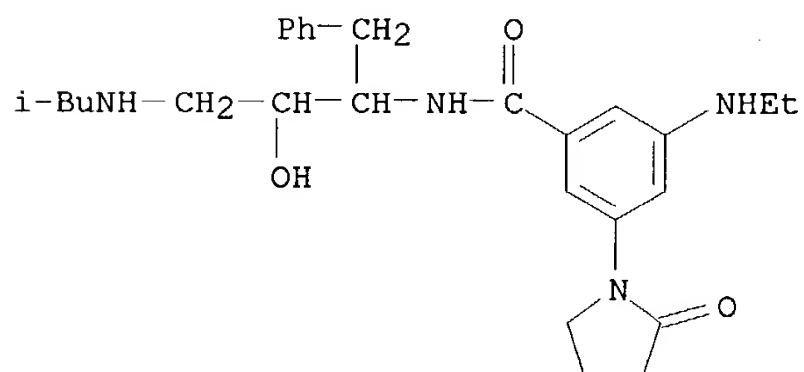
09/895,871

RN 706796-54-5 CAPLUS
CN Benzamide, N-[(1S,2R)-3-[(1,1-dimethylethyl)amino]-2-hydroxy-1-(phenylmethyl)propyl]-3-(ethylamino)-5-(2-oxo-1-pyrrolidinyl)- (9CI) (CA INDEX NAME)

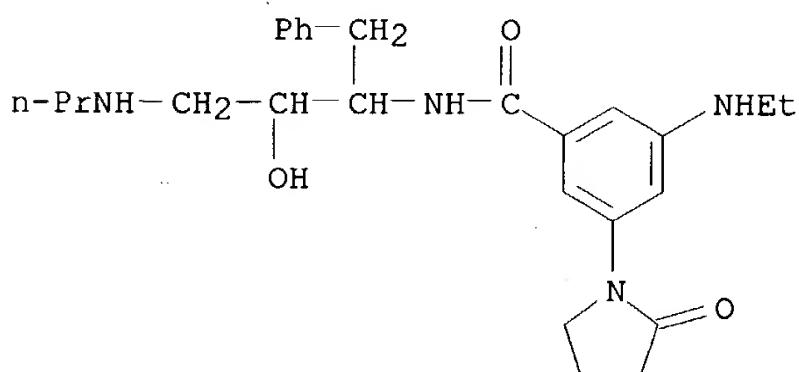
Absolute stereochemistry.



RN 706796-69-2 CAPLUS
CN Benzamide, 3-(ethylamino)-N-[2-hydroxy-3-[(2-methylpropyl)amino]-1-(phenylmethyl)propyl]-5-(2-oxo-1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



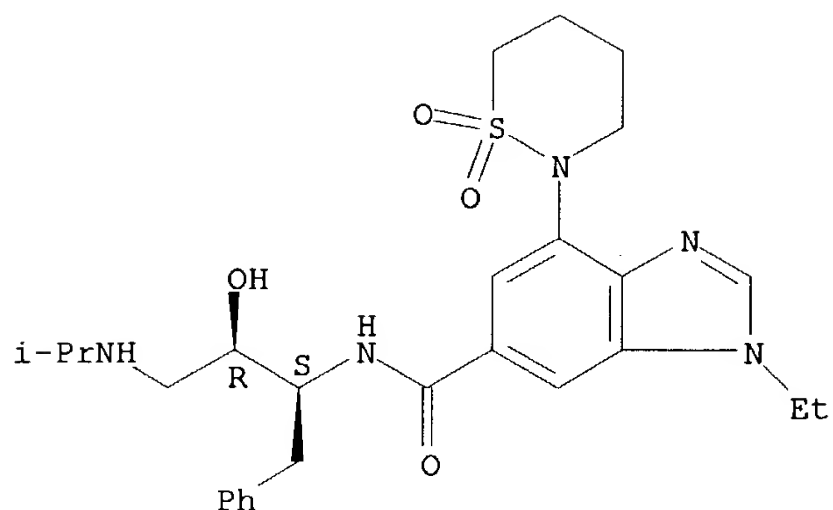
RN 706796-71-6 CAPLUS
CN Benzamide, 3-(ethylamino)-N-[2-hydroxy-1-(phenylmethyl)-3-(propylamino)propyl]-5-(2-oxo-1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



RN 706797-99-1 CAPLUS
CN 1H-Benzimidazole-6-carboxamide, 1-ethyl-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-4-(tetrahydro-1,1-dioxido-2H-1,2-thiazin-2-yl)- (9CI) (CA INDEX NAME)

09/895,871

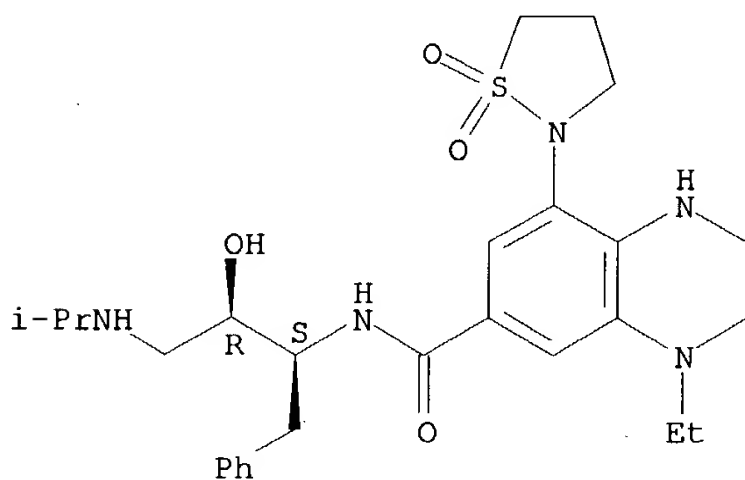
Absolute stereochemistry.



RN 706798-00-7 CAPLUS

CN 6-Quinoxalinecarboxamide, 8-(1,1-dioxido-2-isothiazolidinyl)-4-ethyl-1,2,3,4-tetrahydro-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

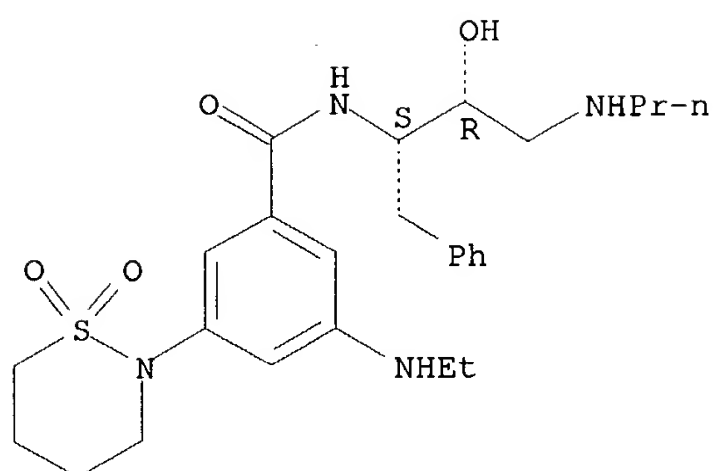


RN 706799-04-4 CAPLUS

CN Benzamide, 3-(ethylamino)-N-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-(propylamino)propyl]-5-(tetrahydro-1,1-dioxido-2H-1,2-thiazin-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

09/895,871

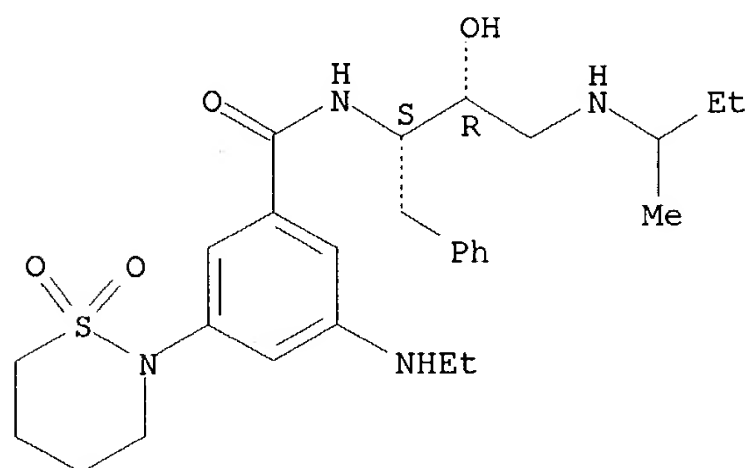


● HCl

RN 706799-09-9 CAPLUS

CN Benzamide, 3-(ethylamino)-N-[(1S,2R)-2-hydroxy-3-[(1-methylpropyl)amino]-1-(phenylmethyl)propyl]-5-(tetrahydro-1,1-dioxido-2H-1,2-thiazin-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



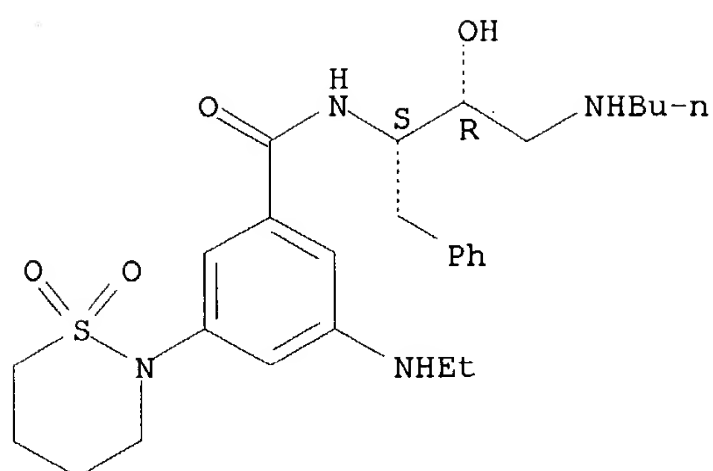
● HCl

RN 706800-33-1 CAPLUS

CN Benzamide, N-[(1S,2R)-3-(butylamino)-2-hydroxy-1-(phenylmethyl)propyl]-3-(ethylamino)-5-(tetrahydro-1,1-dioxido-2H-1,2-thiazin-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

09/895,871



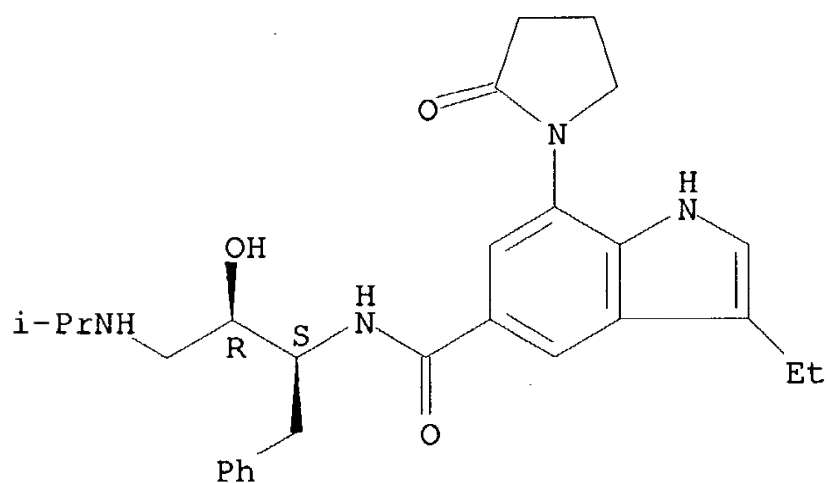
● HCl

RN 706801-48-1 CAPLUS
CN Formic acid, compd. with 3-ethyl-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-7-(2-oxo-1-pyrrolidinyl)-1H-indole-5-carboxamide (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 706801-47-0
CMF C28 H36 N4 O3

Absolute stereochemistry.



CM 2

CRN 64-18-6
CMF C H2 O2

O=CH-OH

RN 706801-59-4 CAPLUS
CN Formic acid, compd. with 7-(1,1-dioxido-2-isothiazolidinyl)-3-ethyl-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-1H-indole-5-carboxamide (1:1) (9CI) (CA INDEX NAME)

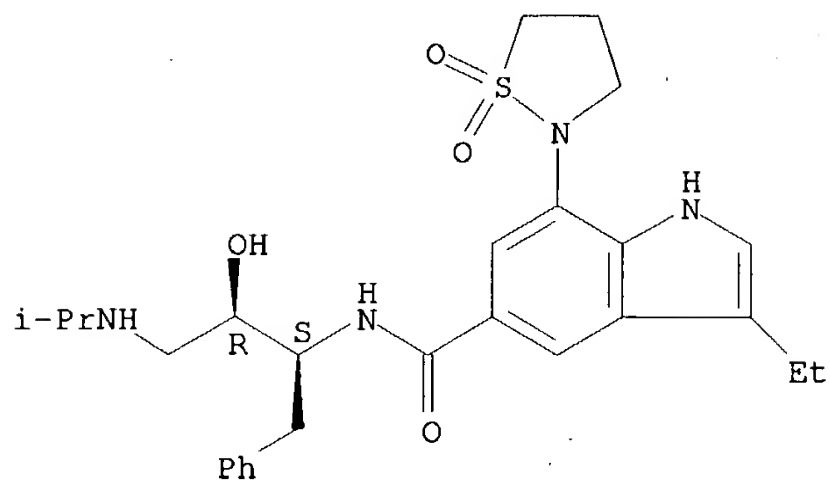
09/895,871

CM 1

CRN 706801-58-3

CMF C27 H36 N4 O4 S

Absolute stereochemistry.



CM 2

CRN 64-18-6

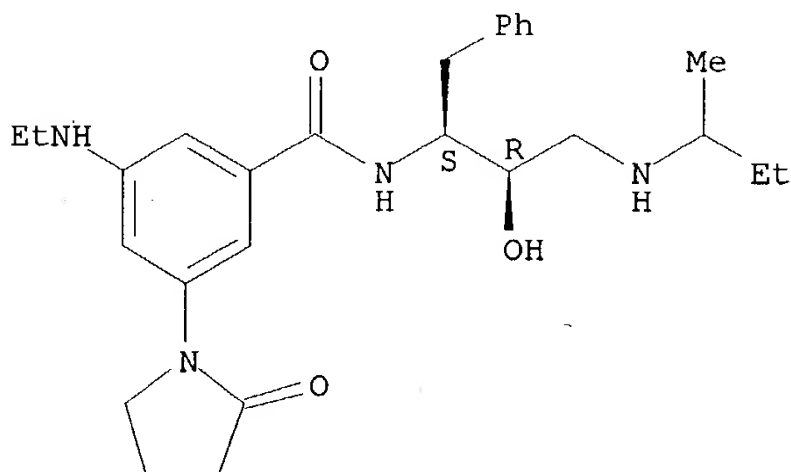
CMF C H2 O2

O=CH-OH

RN 706801-64-1 CAPLUS

CN Benzamide, 3-(ethylamino)-N-[(1S,2R)-2-hydroxy-3-[(1-methylpropyl)amino]-1-(phenylmethyl)propyl]-5-(2-oxo-1-pyrrolidinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 706801-96-9 CAPLUS

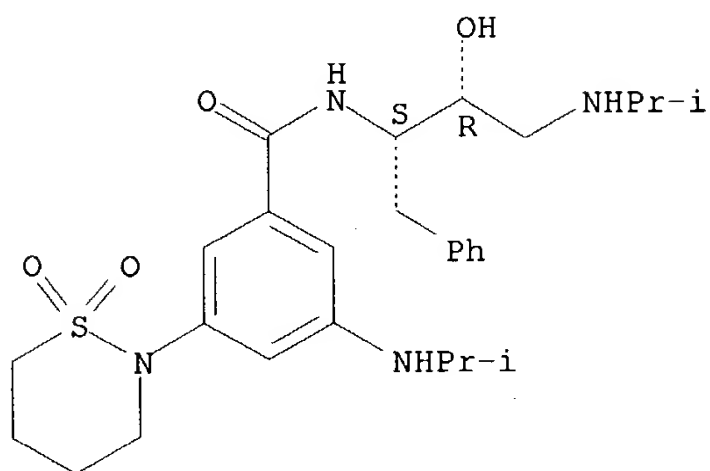
CN Formic acid, compd. with N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-3-[(1-methylethyl)amino]-5-(tetrahydro-1,1-dioxido-2H-1,2-thiazin-2-yl)benzamide (1:1) (9CI) (CA INDEX NAME)

CM 1

09/895,871

CRN 706801-95-8
CMF C27 H40 N4 O4 S

Absolute stereochemistry.



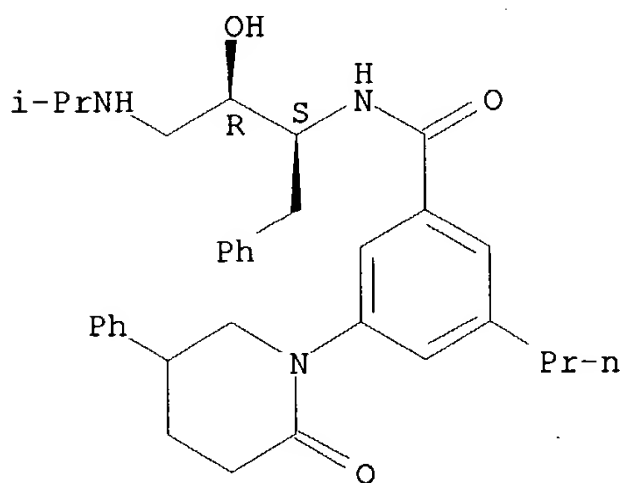
CM 2

CRN 64-18-6
CMF C H2 O2

O=CH-OH

RN 706802-41-7 CAPLUS
CN Benzamide, N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-3-(2-oxo-5-phenyl-1-piperidinyl)-5-propyl- (9CI)
(CA INDEX NAME)

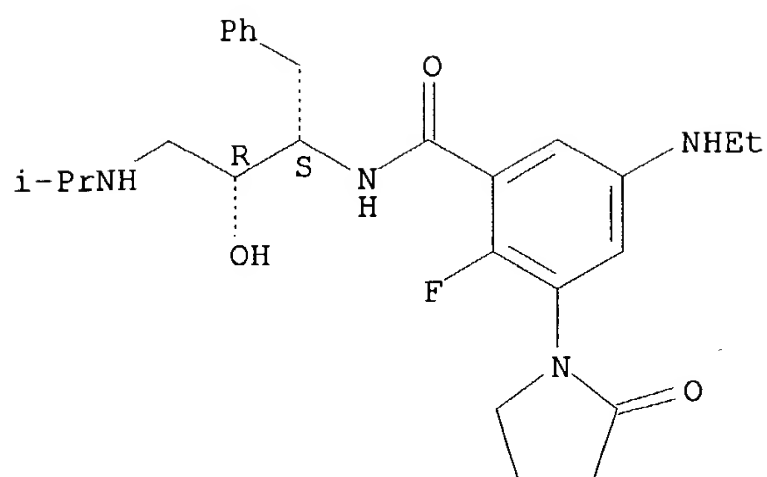
Absolute stereochemistry.



RN 706802-47-3 CAPLUS
CN Benzamide, 5-(ethylamino)-2-fluoro-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-3-(2-oxo-1-pyrrolidinyl)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

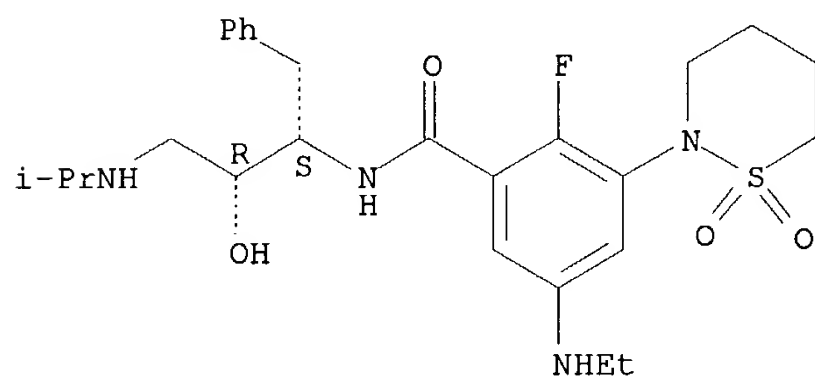
09/895,871



RN 706802-58-6 CAPLUS

CN Benzamide, 5-(ethylamino)-2-fluoro-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-3-(tetrahydro-1,1-dioxido-2H-1,2-thiazin-2-yl)- (9CI) (CA INDEX NAME)

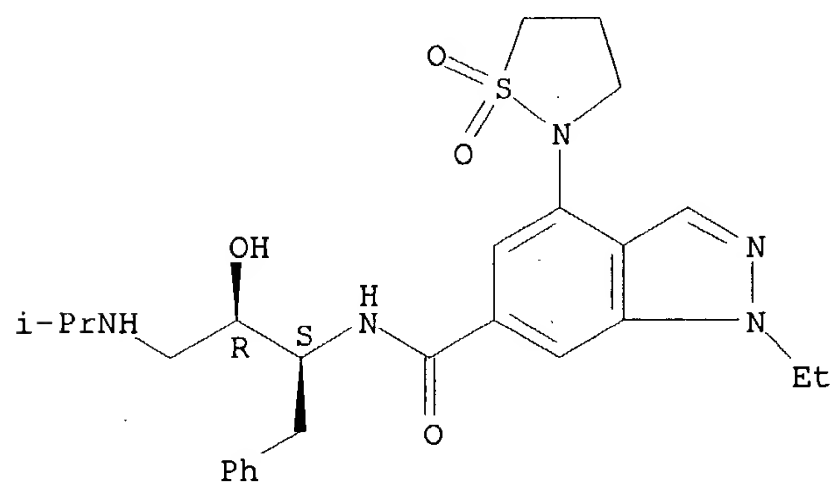
Absolute stereochemistry.



RN 706802-75-7 CAPLUS

CN 1H-Indazole-6-carboxamide, 4-(1,1-dioxido-2-isothiazolidinyl)-1-ethyl-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

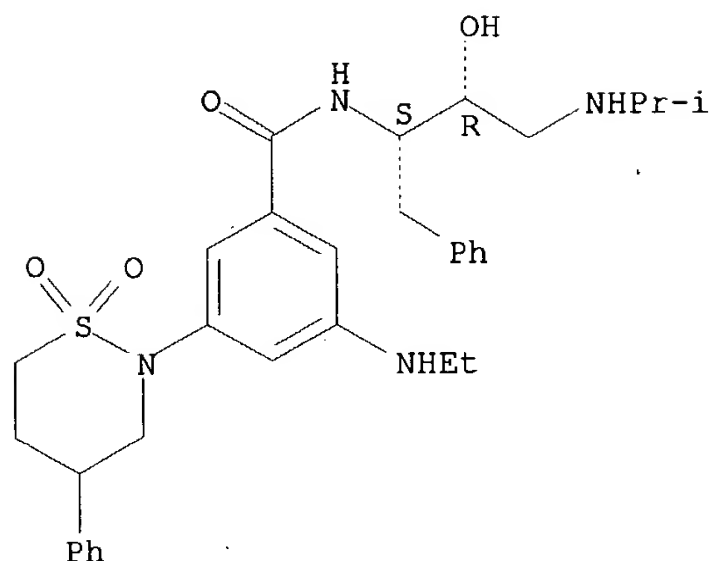


RN 706804-22-0 CAPLUS

CN Benzamide, 3-(ethylamino)-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-5-(tetrahydro-1,1-dioxido-4-phenyl-2H-1,2-thiazin-2-yl)- (9CI) (CA INDEX NAME)

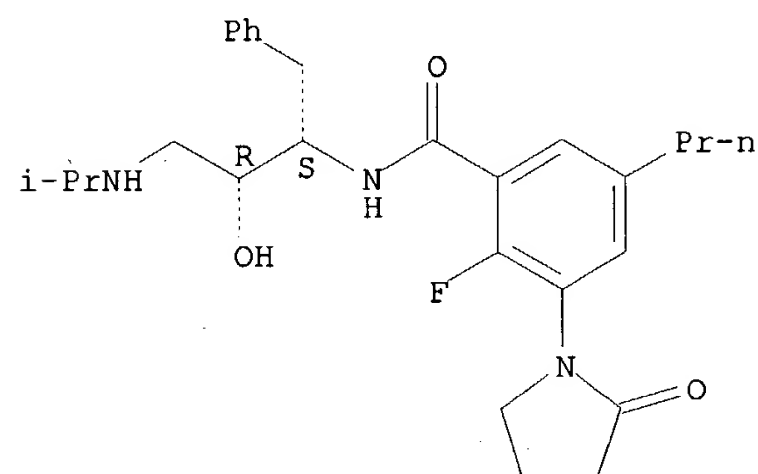
09/895,871

Absolute stereochemistry.



RN 706805-16-5 CAPLUS
CN Benzamide, 2-fluoro-N-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-3-(2-oxo-1-pyrrolidinyl)-5-propyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:696859 CAPLUS
DOCUMENT NUMBER: 139:230480
TITLE: Preparation of substituted amines prodrugs useful in treating Alzheimer's disease
INVENTOR(S): Varghese, John; Jagodzinska, Barbara; Maillard, Michel; Beck, James P.; Tenbrink, Ruth E.; Getman, Daniel
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn
SOURCE: PCT Int. Appl., 483 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072535	A2	20030904	WO 2003-US7287	20030227
WO 2003072535	C1	20040930		

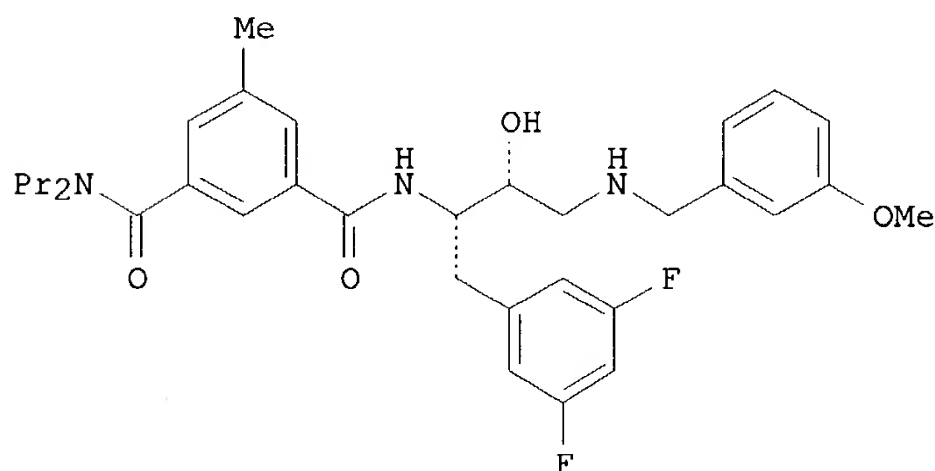
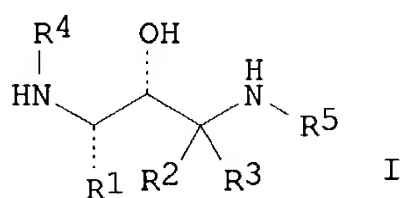
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-359953P P 20020227

OTHER SOURCE(S): MARPAT 139:230480

GI



AB Amines [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, (un)substituted alkyl, alkenyl, etc.; R3 = H, (un)substituted alkyl, alkenyl, etc.; R4 = XR; X = CO, SO₂, a bond, etc.; R = Ph, naphthyl, indanyl, etc.; R5 = (un)substituted alkyl, (CH₂)₀₋₃cycloalkyl, etc.; e.g. N1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-methyl-N3,N3-dipropylisophthalamide], useful in treating Alzheimer's disease and other similar diseases, were prepared. Although the methods of preparation are not claimed, hundreds of example preps. are included. Thus, reacting (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol trifluoroacetate with 5-methyl-N,N-dipropylisophthamic acid in the presence of Et₃N, 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in DMF afforded (1S,2R)-II (N1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-methyl-N3,N3-dipropylisophthalamide). The compds. I exhibit an IC₅₀ of < 50 μM against β-secretase.

IT **388062-20-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(isopropylamino)propyl]-N',N'-dipropylisophthalamide **388062-33-7P**, N-[(1S,2R)-1-Benzyl-3-(butylamino)-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-99-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(isobutylamino)propyl]-N',N'-dipropylisophthalamide **388063-39-6P**, N-[(1S,2R)-3-(Butylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388065-53-0P**, N-[(1S,2R)-3-(Butylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-ethynyl-N',N'-dipropylisophthalamide **590423-35-1P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-(isobutylamino)propyl]-5-methyl-N',N'-dipropylisophthalamide

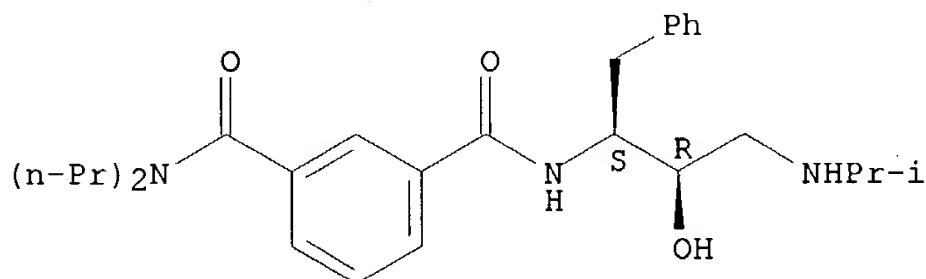
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of substituted amine prodrugs useful in treating Alzheimer's disease)

RN 388062-20-2 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

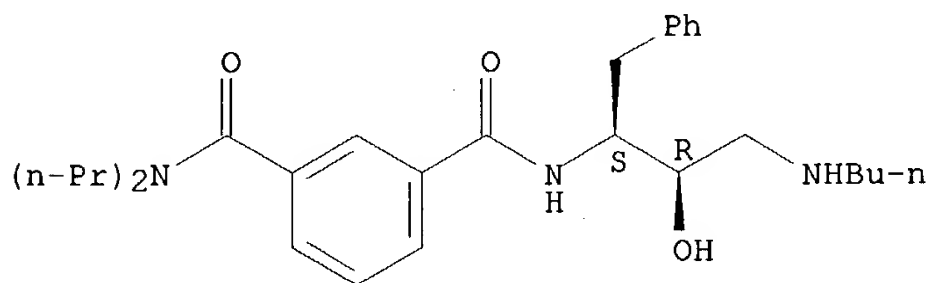
Absolute stereochemistry.



RN 388062-33-7 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-(butylamino)-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

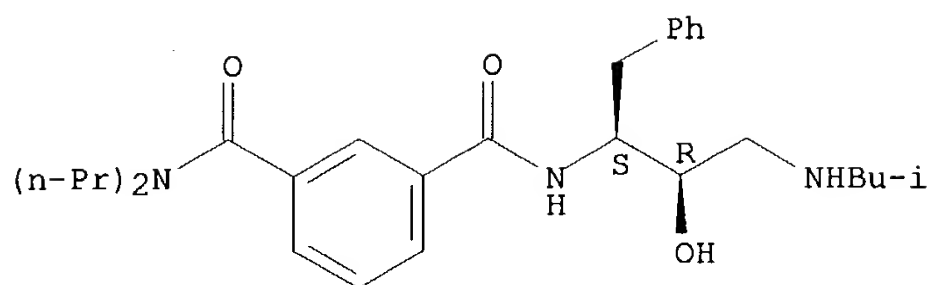


RN 388062-99-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[(2-methylpropyl)amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

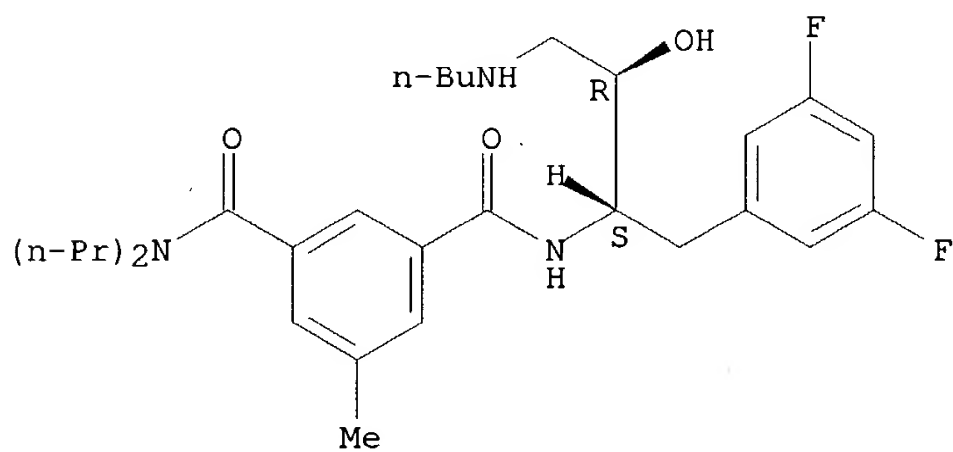
09/895,871



RN 388063-39-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-(butylamino)-1-[(3,5-difluorophenyl)methyl]-2-hydroxypropyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

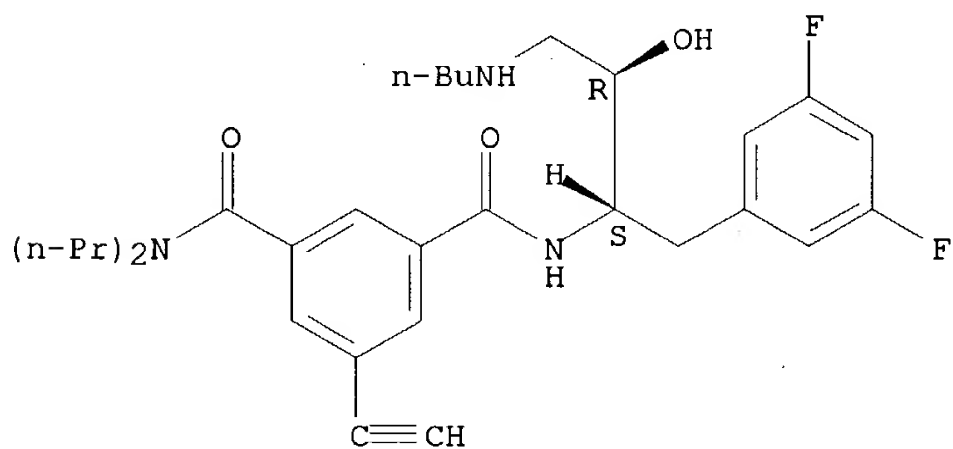
Absolute stereochemistry.



RN 388065-53-0 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-(butylamino)-1-[(3,5-difluorophenyl)methyl]-2-hydroxypropyl]-5-ethynyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

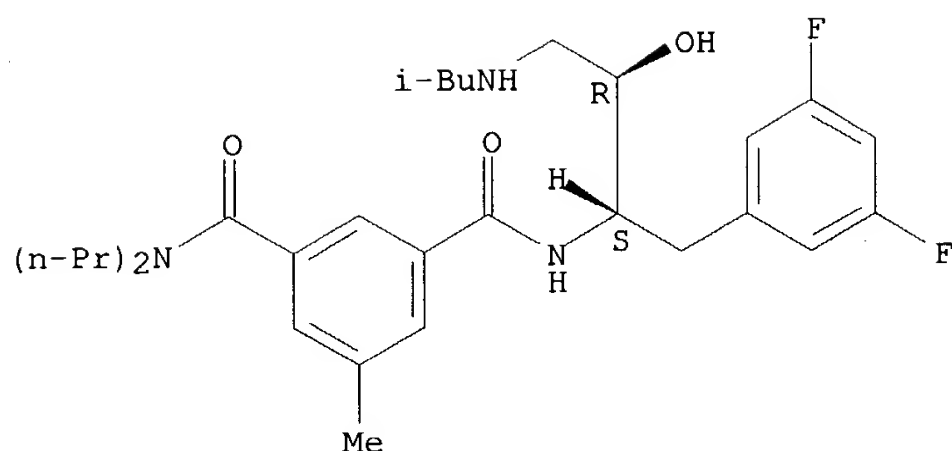
Absolute stereochemistry.



RN 590423-35-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[(2-methylpropyl)amino]propyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:412801 CAPLUS

DOCUMENT NUMBER: 139:245782

TITLE: Preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease

INVENTOR(S): Varghese, John; Maillard, Michel; Jagodzinska, Barbara; Beck, James P.; Gailunas, Andrea; Fang, Larry; Sealy, Jennifer; Tenbrink, Ruth; Freskos, John; Mickelson, John; Samala, Lakshman; Hom, Roy

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company

SOURCE: PCT Int. Appl., 1243 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040096	A2	20030515	WO 2002-XA36072	20021108
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2003040096	A2	20030515	WO 2002-US36072	20021108
WO 2003040096	A3	20040506		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

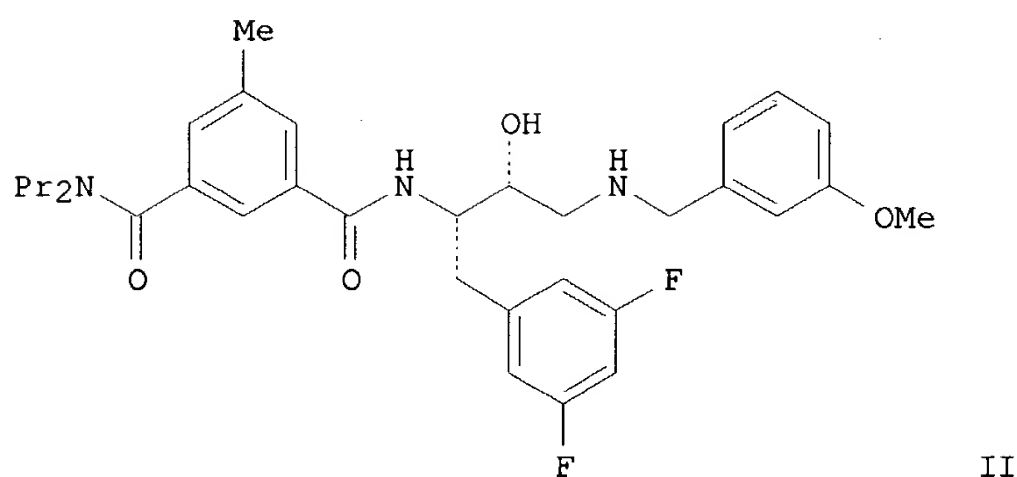
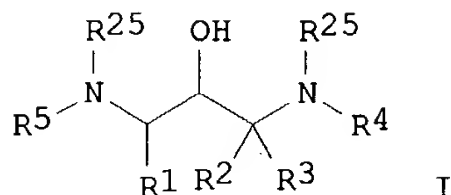
PRIORITY APPLN. INFO.:

US 2001-337122P

P 20011108

US 2001-344086P P 20011228
 US 2002-345635P P 20020103
 WO 2002-US36072 A 20021108

OTHER SOURCE(S): MARPAT 139:245782
 GI



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, alkyl, haloalkyl, alkenyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; or R2 and R3 are taken together with the carbon to which they are attached to form a carbocycle of 3-7 carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of O, S, SO₂, (un)substituted NH; R4 = alkyl, haloalkyl, hydroxyalkyl, etc.; R5 = R6X (wherein X = CO, SO₂, (un)substituted CH₂; R6 = (un)substituted Ph, naphthyl, indanyl, etc.); R25 = H, alkyl, alkoxy, etc.] which have activity as inhibitors of β -secretase and are therefore useful in treating a variety of disorders such as Alzheimer's disease, were prepared E.g., a multi-step synthesis of (1S,2R)-II, starting from (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5-difluorophenyl)propanoic acid, was given. The compds. I showed IC₅₀ of < 20 μ M in cell free inhibition assay utilizing a synthetic APP substrate. This is a Part 2 of 1-2 series.

IT **597559-81-4P**

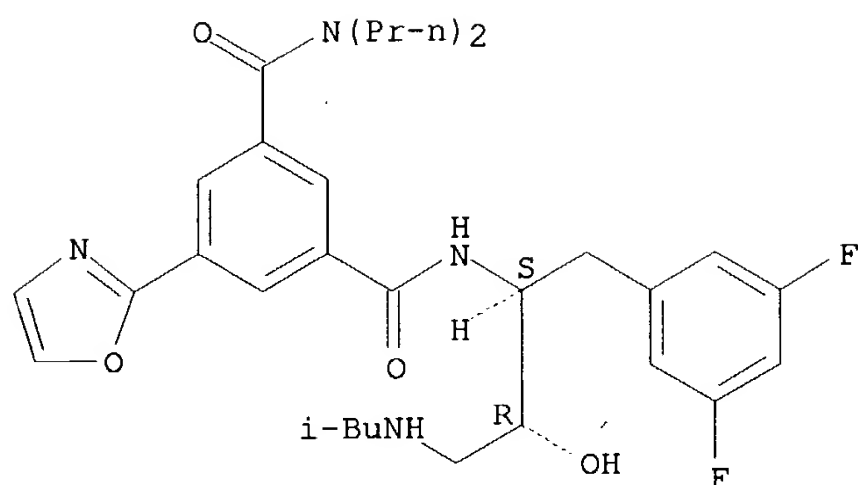
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease)

RN 597559-81-4 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[(2-methylpropyl)amino]propyl]-5-(2-oxazolyl)-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:376819 CAPLUS

DOCUMENT NUMBER: 138:385173

TITLE: Preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease

INVENTOR(S): Varghese, John; Maillard, Michel; Jagodzinska, Barbara; Beck, James P.; Gailunas, Andrea; Fang, Larry; Sealy, Jennifer; Tenbrink, Ruth; Freskos, John; Mickelson, John; Samala, Lakshman; Hom, Roy

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company

SOURCE: PCT Int. Appl., 1243 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

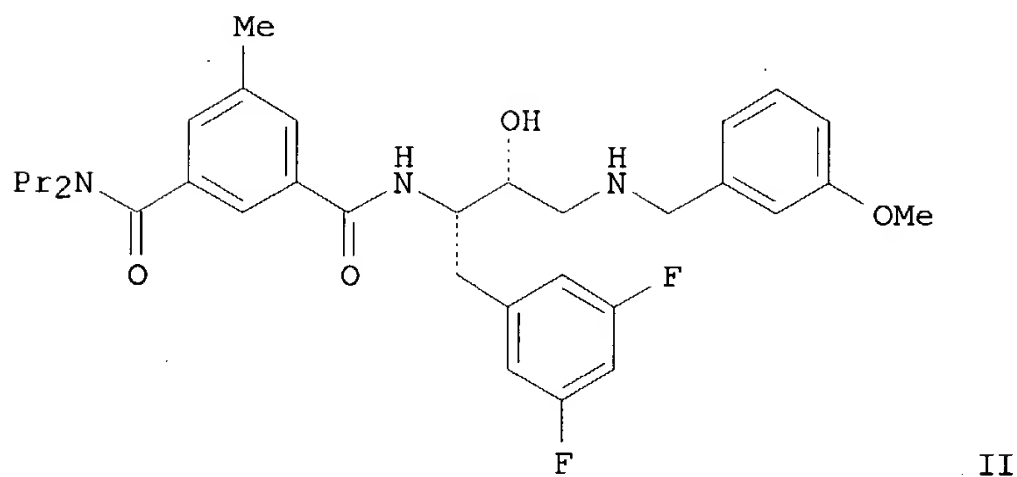
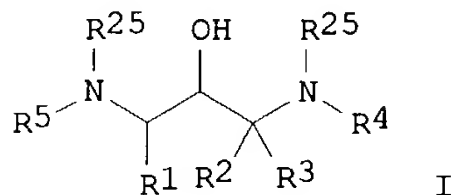
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040096	A2	20030515	WO 2002-US36072	20021108
WO 2003040096	A3	20040506		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2003040096	A2	20030515	WO 2002-XA36072	20021108
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

09/895,871

US 2004171881 A1 20040902 US 2002-291318 20021108
EP 1453789 A2 20040908 EP 2002-793909 20021108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
PRIORITY APPLN. INFO.: US 2001-337122P P 20011108
US 2001-344086P P 20011228
US 2002-345635P P 20020103
WO 2002-US36072 A 20021108
OTHER SOURCE(S): MARPAT 138:385173
GI



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, alkyl, haloalkyl, alkenyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; or R2 and R3 are taken together with the carbon to which they are attached to form a carbocycle of 3-7 carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of O, S, SO₂, (un)substituted NH; R4 = alkyl, haloalkyl, hydroxyalkyl, etc.; R5 = R6X (wherein X = CO, SO₂, (un)substituted CH₂; R6 = (un)substituted Ph, naphthyl, indanyl, etc.); R25 = H, alkyl, alkoxy, etc.] which have activity as inhibitors of β -secretase and are therefore useful in treating a variety of disorders such as Alzheimer's disease, were prepared E.g., a multi-step synthesis of (1S,2R)-II, starting from (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5-difluorophenyl)propanoic acid, was given. The compds. I showed IC₅₀ of < 20 μ M in cell free inhibition assay utilizing a synthetic APP substrate. This is a Part 1 of 1-2 series.

IT 527718-24-7P 527726-59-6P 527727-51-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

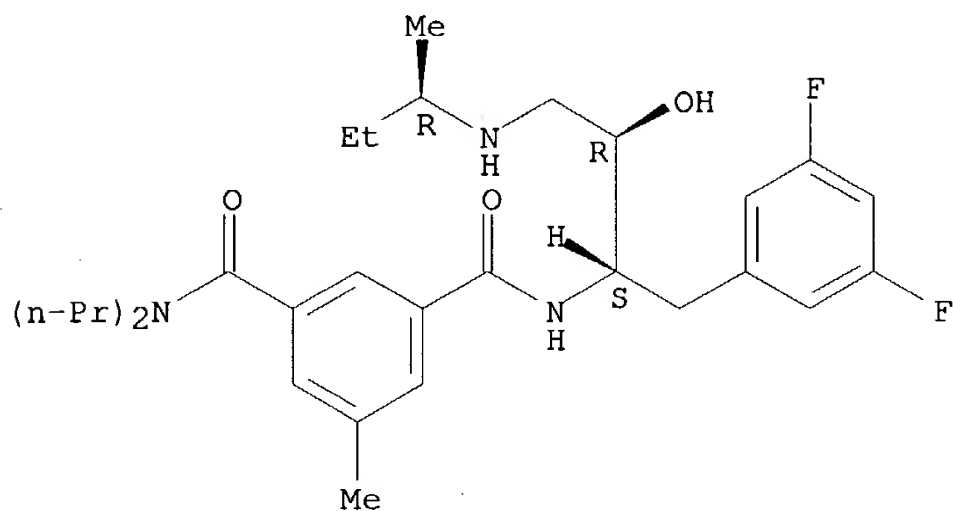
(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease)

RN 527718-24-7 CAPLUS

09/895,871

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[(1R)-1-methylpropyl]amino]propyl]-5-methyl-N,N-dipropyl- (9CI)
(CA INDEX NAME)

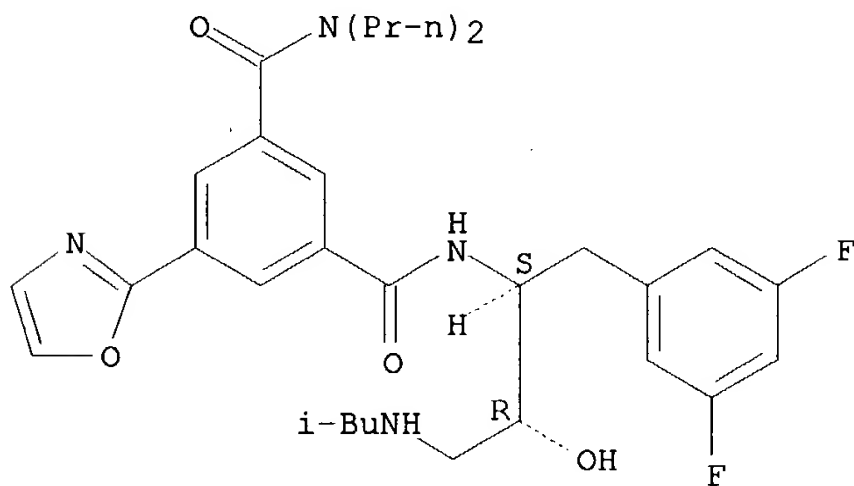
Absolute stereochemistry.



RN 527726-59-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[(2-methylpropyl)amino]propyl]-5-(2-oxazolyl)-N,N-dipropyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

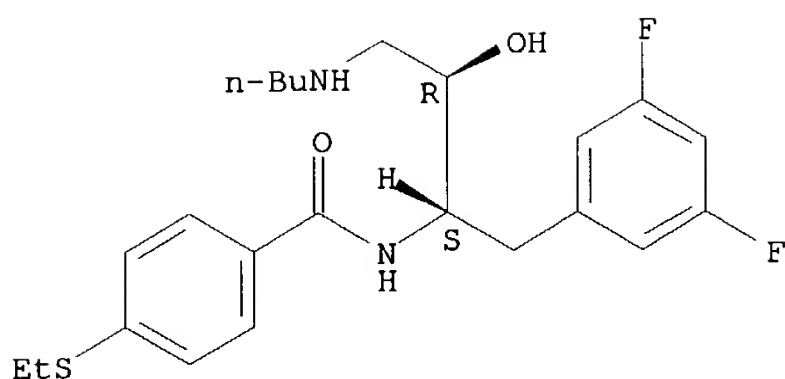


● HCl

RN 527727-51-1 CAPLUS

CN Benzamide, N-[(1S,2R)-3-(butylamino)-1-[(3,5-difluorophenyl)methyl]-2-hydroxypropyl]-4-(ethylthio)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:31402 CAPLUS

DOCUMENT NUMBER: 136:102190

TITLE: Preparation of substituted amines to treat Alzheimer's disease

INVENTOR(S): Maillaird, Michel; Hom, Court; Gailunas, Andrea; Jagodzinska, Barbara; Fang, Lawrence Y.; John, Varghese; Freskos, John N.; Pulley, Shon R.; Beck, James P.; Tenbrink, Ruth E.

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company

SOURCE: PCT Int. Appl., 651 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

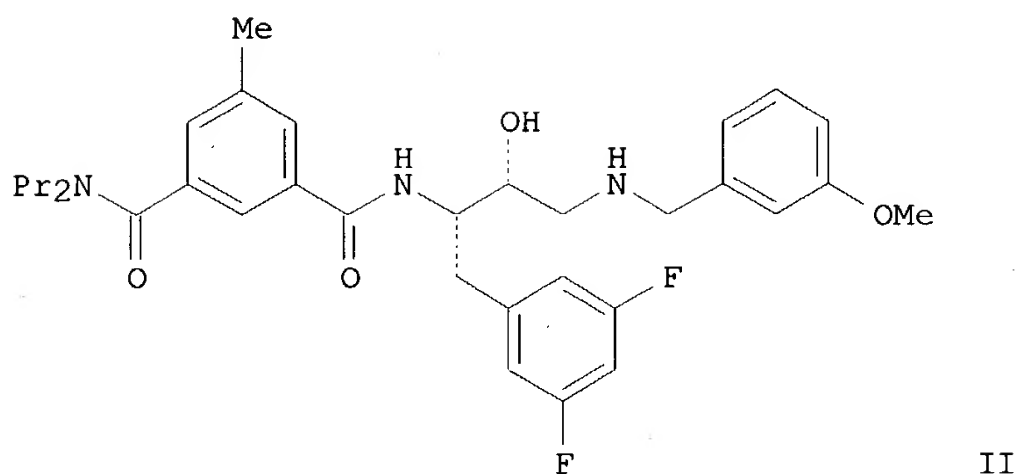
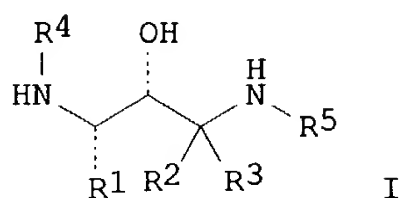
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002512	A2	20020110	WO 2001-US21012	20010629
WO 2002002512	A3	20030821		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2410651	AA	20020110	CA 2001-2410651	20010629
AU 2001073137	A5	20020114	AU 2001-73137	20010629
US 2002128255	A1	20020912	US 2001-896139	20010629
BR 2001012000	A	20030603	BR 2001-12000	20010629
EP 1353898	A2	20031022	EP 2001-952378	20010629
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004502669	T2	20040129	JP 2002-507769	20010629
EE 200200716	A	20040816	EE 2002-716	20010629
NO 2002006199	A	20030221	NO 2002-6199	20021223
PRIORITY APPLN. INFO.:				
			US 2000-215323P	P 20000630
			US 2000-252736P	P 20001122
			US 2000-255956P	P 20001215
			US 2001-268497P	P 20010213
			US 2001-279779P	P 20010329

09/895,871

US 2001-295589P
WO 2001-US21012

P 20010604
W 20010629

OTHER SOURCE(S): MARPAT 136:102190
GI



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, (un)substituted alkyl, alkenyl, etc.; R3 = H, (un)substituted alkyl, alkenyl, etc.; R4 = XR; X = CO, SO₂, a bond, etc.; R = Ph, naphthyl, indanyl, etc.; R5 = (un)substituted alkyl, (CH₂)₀₋₃cycloalkyl, etc.], useful in treating Alzheimer's disease and other similar diseases, were prepared Thus, reacting (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol trifluoroacetate with 5-methyl-N,N-dipropylisophthalamide in the presence of Et₃N, 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in DMF afforded (1S,2R)-II. The compds. I exhibit an IC₅₀ of < 50 μM against beta-secretase.

IT 388062-20-2P 388062-33-7P 388062-99-5P
388063-39-6P 388065-53-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

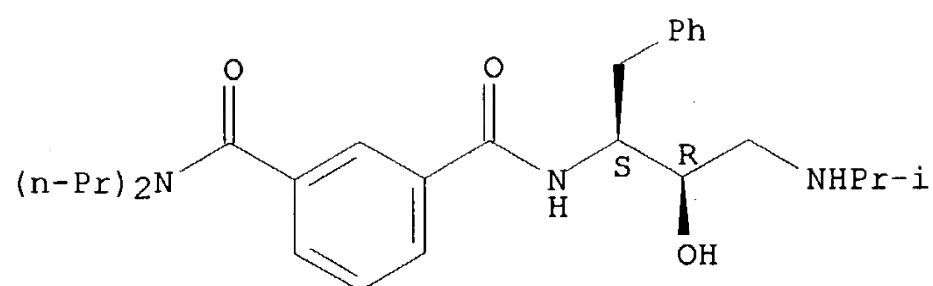
(preparation of substituted amines for treating Alzheimer's disease)

RN 388062-20-2 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

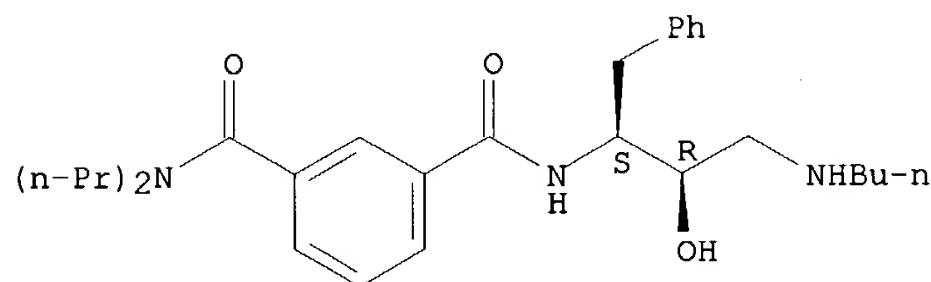
09/895,871



RN 388062-33-7 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-(butylamino)-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

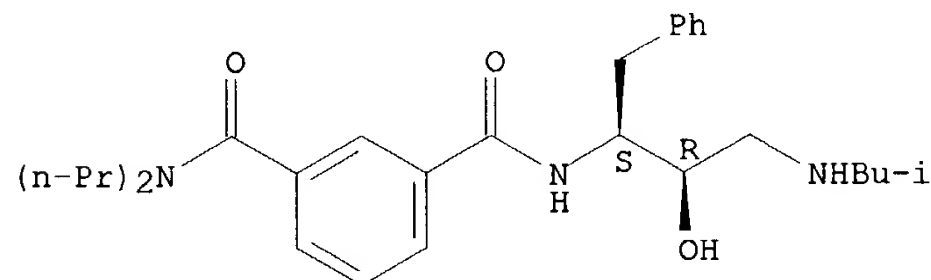
Absolute stereochemistry.



RN 388062-99-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[(2-methylpropyl)amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

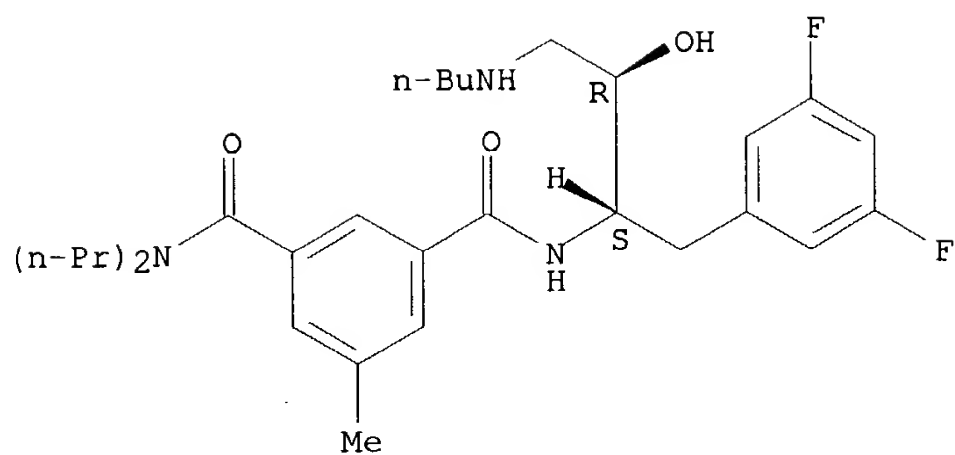


RN 388063-39-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-(butylamino)-1-[(3,5-difluorophenyl)methyl]-2-hydroxypropyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

09/895,871



RN 388065-53-0 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-(butylamino)-1-[(3,5-difluorophenyl)methyl]-2-hydroxypropyl]-5-ethynyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

